CHEM 2P21
Information Exercise
Winter 2014 term

Ian Gordon

Ian Gordon, Teaching & Learning Librarian

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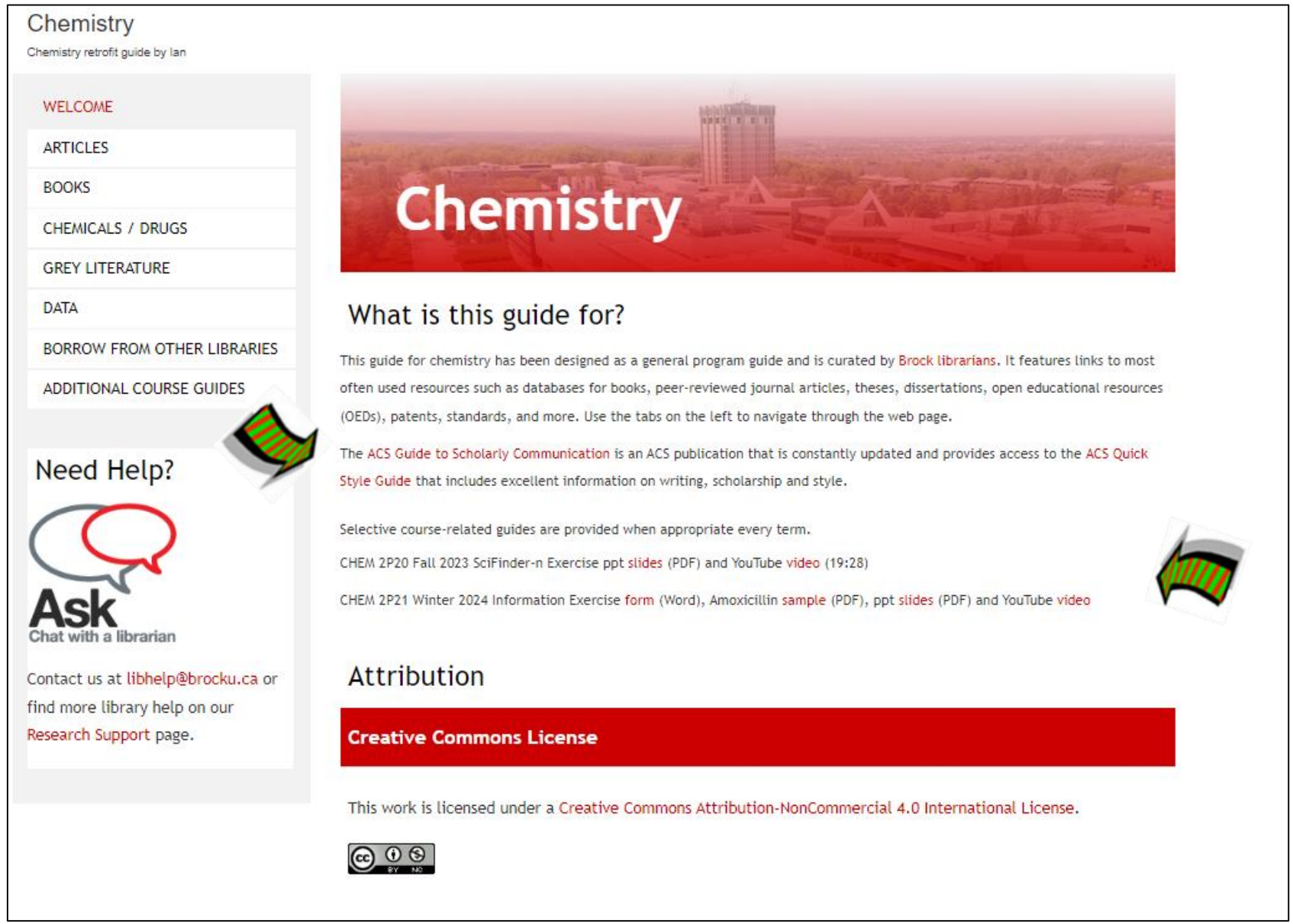
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Chemistry
What is this guide for?
This guide for chemistry has been designed as a general program guide and is curated by Brock librarians. It features links to most often used resources such as databases for books, peer-reviewed journal articles, theses, dissertations, open educational resources (OEDs), patents, standards, and more. Use the tabs on the left to navigate through the web page.
The ACS Guide to Scholarly Communication is an ACS publication that is constantly updated and provides access to the ACS Quick Style Guide that includes excellent information on writing, scholarship and style.
Selective course-related guides are provided when appropriate every term.
CHEM 2P20 Fall 2023 SciFinder-n Exercise ppt slides (PDF) and YouTube video (19:28)
CHEM 2P21 Winter 2024 Information Exercise form (Word), Amoxicillin sample (PDF), ppt slides (PDF) and YouTube video
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CHEM 2P21 Information Exercise Winter 2024

The objective of this exercise is to explore the scholarly biomedical, chemistry, green and patent literature. This exercise involves searching the chemistry literature in different ways looking for information, articles and patents using unique chemistry- and open-oriented databases. Note the Brock Library Chemistry and Biochemistry Library Research Guides for assistance.

Select **one** antifungal or antibiotic drug from these sites or one listed below for this assignment: Antifungal (Wikipedia), What are the most common antibiotics? (healthline), Azithromycin, Cephalexin, Ciprofloxacin, Clindamycin, Clarithromycin, Doxycycline, Levofloxacin, Meropenem, Metronidazole, Sulfamethoxazole, or Tobramycin.

Consider learning more about your drug/chemical using a variety of chemistry databases and catalogs including: ChEMBL, ChEBI, ChemID Plus (NIH), DrugBank, Drugs.com, NCBI Chemicals & Bioassays (NIH), fisherscientific, Sigma-Aldrich, and RxList.

Use Zotero or zoterobib to create citations using American Chemical Society style. The ACS Guide to Scholarly Communication is an ACS publication that is constantly updated and provides access to the ACS Quick Style Guide that includes excellent information on writing, scholarship and style.

1. Complete the following for your small chemical / antibiotic / drug of choice using SciFinder-n:

   Chemical / Drug name: Molecular Formula (using the Hill System):
   CAS Registry Number: IUPAC Name:

   Insert **one** interesting image of your drug's chemical structure and name the source.

   _____

2. Comment on this drug's cost and availability using a commercial supplier e.g. Sigma-Aldrich, Chemical Book, or use the SciFinder-n "Commercial Sources" tab, and comment whether it would be cheaper/easier to make the drug or purchase it yourself? Briefly, please explain why.

   _____

3. In two or three sentences explain why this chemical/drug is important summarizing its bioactivity, chemical drug classification, bioactivity, target indicator, mode of action and how it works as an antibiotic/antibacterial drug.

   _____

4. Go to the SciFinder-n database. You need to register for a new or remember your personal SciFinder-n account username/password. Contact help@cas.org if needed. Complete the following:

   How many retrieved reactions searching your drug as a product? ___
   How many retrieved reactions searching your drug as a drawn structure? ___
   How many retrieved Results when searching your drug name and the keyword prepar* in Reference titles? ___
   How many of these references are patents? Document Type = Patent? ___

   Sort citations by relevance, yield, number of steps, date, relevance… Select the most recent or one of the most interesting patents, check out the citation, indexing, click on PatentPak and Full Text, and cite it below using ACS Citation (with title) style:

5. Go to PubChem, find your drug, check out all contents, completing the following:

   What is the PubChem CID for your drug? ___
   What is the next highest MeSH and Thesaurus Tree classification names for your drug?
   _____

6. Go to the Reaxys database (no registration needed). Do a "Quick search" which is the default setting. Search for your drug, view the most appropriate entry, indicate:

   What is the Reaxys ID number for your drug? ___
   Number of Reaxys preparations ___, documents ___, and reactions ___
   Click on the Retrosynthesis tab at the top of the Reaxys search page, look up your compound and run your synthesis which takes all reactions, variant compounds and then looks to produce an algorithmically AI search reaction tree complete with experimental procedures when available for your benefit. View the future of synthetic organic chemistry that will soon AI data to run biological sequences, target groups, steps, reactions… all linked to article and patent citations.
   How many published retrosynthesis did Reaxys find? ___

7. Using Reaxys, click on new search, do a "Query builder" search this time which guides you through a search strategy one step at a time. Search for your drug (e.g. CAS no.), select "Search in: Reactions", filter/limit to "Yield", filter/limit to Document Type "article", sort by "Reaxys ranks" and pick one of the current or most interesting articles.

   What is this reaction yield ___**%** and include the citation using ACS Citation (with title) style.

   _____

8. Using Reaxys, click on "Quick search", type in your patent citation used in question number 4, find the Reaxys citation, click on Full Text, which takes you to the Espacenet database. This is an amazing database published by the European Union. How many claims for this patent? ___

   In one or two sentences what is novel or unique about this patent and these claim(s)?

   _____

9. You've been hired by an international pharmaceutical company as a researcher / chemist / scientist and challenged to respond to the CDC's 2019 AR Threats Report. Read the entire document! Using your favorite scholarly database, find a recent scholarly peer-reviewed experimental biochemistry, biological, pharmacology, biomedical, or chemistry journal article **using one of the 18 antibiotic-resistant bacteria or fungi** that speaks to this threat. This article has to include experimental methodology and data to answer question 10. Cite this paper using ACS Citation (with title):

   _____

10. In one or two sentences, use your own words to comment on whether the paper you picked for Question number 9's methodology, reactions, data, and techniques are (or are not) indicative of the 12 Principles of Green Chemistry.

    _____

Kuprienko, O. S.; Serchenya, T. S.; Vashkevich, I. I.; Harl
Conjugates of Aminopenicillins with Proteins: Synthesis
the β-Lactam Receptor and Antibodies. Russ J Bioorg C
https://doi.org/10.1134/S106816202201006X

8. Using Reaxys, click on "Quick search", type in your pate
the Reaxys citation, click on Full Text, which takes you t
amazing database publish——ed by the European Unio

   In one or two sentences what is novel or unique about

   **This patent claims a new method for the preparation
   including Amoxicillin based on previous patents and r
   derivatives, salts, and processes in the presence of ur
   unique formulations and experimental conditions.**

9. You've been hired by an international pharmaceutical
and challenged to respond to the CDC's 2019 AR Threa
your favorite scholarly database, find a recent scholarly
biological, pharmacology, biomedical, or chemistry jou
resistant bacteria or fungi that speaks to this threat. T
methodology and data to answer question 10. Cite the
name, and the article found using ACS Citation (with tit

   Selected Web of Science Core Collection database, Sb

   Dhara, D.; Mulard, L. A. Exploratory N-Protecting
   Synthesis of Zwitterionic *Shigella Sonnei* Oligosac
   chem.202003480. DOI:10.1002/chem.202003480.

10. In one or two sentences, use your own words to comm
Question number 9's methodology, reactions, data, an
the 12 Principles of Green Chemistry.

    **I am speaking to "Safer Solvents and Auxiliaries" and
    comments were found in the methodology or results
    fewest life cycle environmental impact or the safe dis
    product Acet/H2O, DCA-Cl, Et3N, CAN, MeOH, THF… s**

Ian Gordon

igordon@brocku.ca

**Depending upon how amoxicillin is formulated as a pharmaceutical dr
$60-$75/gram or $16/5ml suspension 100ml bottle. Noting the aromat
stereochemistry, it would be difficult to formulate and is just too chea**

3. In one or two sentences explain why this chemical/drug is important su
chemical drug classification, bioactivity, target indicator, mode of action
antibiotic/antibacterial drug.

   **Amoxicillin is one of the most popular beta-lactam antibiotics used to
   mainly in children. As a small molecule penicillin organoheterocyclic co
   binds to, weakens and causes cell lysis, inactivating penicillin-binding p
   bacterial cell walls in both negative- and gram- positive bacteria.**

4. Go to the SciFinder-n database. You need a register for a new or remem
SciFinder-n account username/password. Complete the following:

   How many retrieved ***reactions*** searching your drug as a *product*? **189**
   How many retrieved ***reactions*** searching your drug as a drawn structure
   How many retrieved Results when searching your drug name and the ke
   Reference titles? **492**
   How many of these references are patents? Document Type = Patent? **3**

   Sort citations by relevance, yield, number of steps, date, relevance… Sel
   of the most interesting patents, check out the citation, indexing, click or
   and cite it below using ACS Citation (with title) style:

   **Leenderts, E J A. Preparation of beta-lactam antibiotics in the presence
   0953569A1, Nov 3, 1999.**

5. Go to PubChem, find your drug, check out all contents, completing the f

   What is the PubChem CID for your drug? **33613**
   What is the next highest MeSH and Thesaurus Tree classification names
   Amoxicillin is a type of Ampicillin and Penicillin Antibiotic.

6. Go to the Reaxys database (no registration needed). Do a "Quick search
setting. Search for your drug, view the most appropriate entry, indicate

   What is the Reaxys ID number for your drug? **4274654**
   Number of Reaxys preparations **23**, documents **27,230**, and reactions **22**
   Click on the Retrosynthesis tab at the top of the Reaxys search page, loo
   run your synthesis which takes all reactions, variant compounds and the
   algorithmically AI search reaction tree complete with experimental proc
   your benefit. View the future of synthetic organic chemistry that will soo
   sequences, target groups, steps, reactions… all linked to article and pate
   How many published retrosynthesis did Reaxys find? **Five**

7. Using Reaxys, click on new search, do a "Query builder" search this time
a search strategy one step at a time. Search for your drug (e.g. CAS no.),
Reactions", filter/limit to "Yield", filter/limit to Document Type "article"
pick one of the current or most interesting articles.

   What is this reaction yield **76%** and include the citation using ACS Citati

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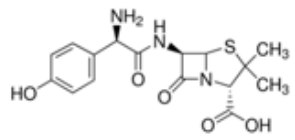
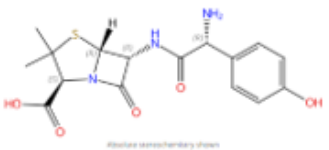
1. Complete the following for your small chemical / antibiotic / drug of choice using SciFinder-n:

   Chemical / Drug name: **Amoxicillin**
   Molecular Formula: **C16 H19 N3 O5 S**
   CAS Registry Number: **26787-78-0**
   IUPAC Name: **(2S,5R,6R)-6-[[(2R)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid**

   Insert one interesting image of your drug's chemical structure and name the source. **Here are two:**



Sigma-Aldrich



ACS SciFinder-n

2. Comment on this drug's cost and availability using a commercial supplier e.g. Sigma-Aldrich, Chemical Book, or use the SciFinder-n "Commercial Sources" tab, and comment whether it would be cheaper/easier to make the drug or purchase it yourself? Explain why.

CHEM 2P21 Information Exercise

- Download Word form to fill in and submit by the due date
- Consult the PDF answers for Amoxicillin for formatting and review
- Select a drug/small chemical compound from the list
- Register for a SciFinder-n account
- All other databases are available through the Brock proxy server
- Do assignment on campus as much as possible
- Be clear and concise when providing answers
- Recognize the value of zoterobib and Zotero citation management software
- Add American Chemical Society formatting style to zoterobib
- Consult the The ACS Guide to Scholarly Communication
- If you book a consultation indicate whether it is a virtual/Teams or in person meeting
- Don’t copy or plagiarize!

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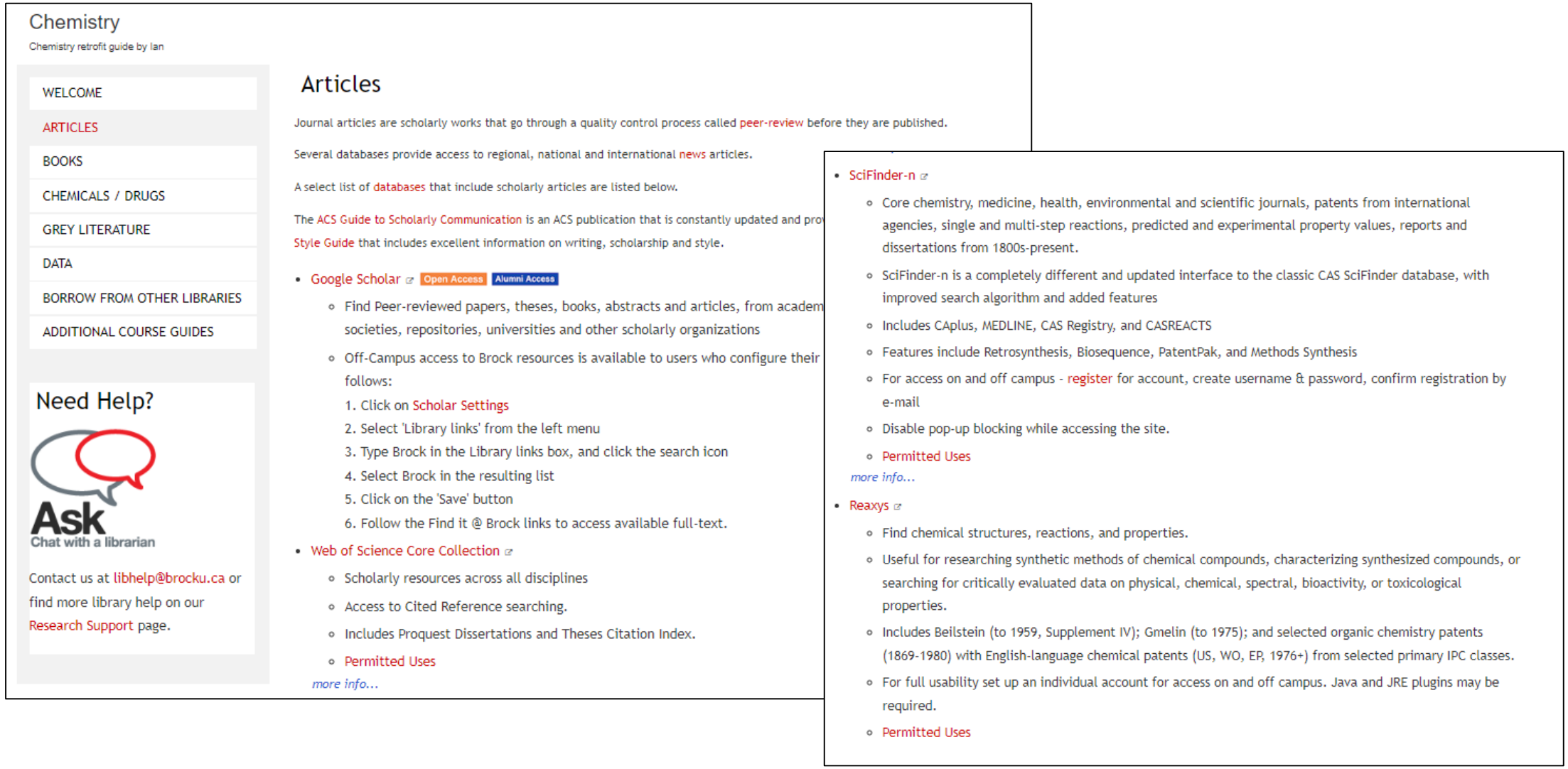

Chemistry

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Articles

Journal articles are scholarly works that go through a quality control process called peer-review before they are published.

Several databases provide access to regional, national and international news articles.

A select list of databases that include scholarly articles are listed below.

The ACS Guide to Scholarly Communication is an ACS publication that is constantly updated and pro
Style Guide that includes excellent information on writing, scholarship and style.

- Google Scholar Open Access Alumni Access
  - Find Peer-reviewed papers, theses, books, abstracts and articles, from academ societies, repositories, universities and other scholarly organizations
  - Off-Campus access to Brock resources is available to users who configure their follows:
    1. Click on Scholar Settings
    2. Select 'Library links' from the left menu
    3. Type Brock in the Library links box, and click the search icon
    4. Select Brock in the resulting list
    5. Click on the 'Save' button
    6. Follow the Find it @ Brock links to access available full-text.
- Web of Science Core Collection
  - Scholarly resources across all disciplines
  - Access to Cited Reference searching.
  - Includes Proquest Dissertations and Theses Citation Index.
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more info...

- SciFinder-n
  - Core chemistry, medicine, health, environmental and scientific journals, patents from international agencies, single and multi-step reactions, predicted and experimental property values, reports and dissertations from 1800s-present.
  - SciFinder-n is a completely different and updated interface to the classic CAS SciFinder database, with improved search algorithm and added features
  - Includes CAplus, MEDLINE, CAS Registry, and CASREACTS
  - Features include Retrosynthesis, Biosequence, PatentPak, and Methods Synthesis
  - For access on and off campus - register for account, create username & password, confirm registration by e-mail
  - Disable pop-up blocking while accessing the site.
  - Permitted Uses

more info...

- Reaxys
  - Find chemical structures, reactions, and properties.
  - Useful for researching synthetic methods of chemical compounds, characterizing synthesized compounds, or searching for critically evaluated data on physical, chemical, spectral, bioactivity, or toxicological properties.
  - Includes Beilstein (to 1959, Supplement IV); Gmelin (to 1975); and selected organic chemistry patents (1869-1980) with English-language chemical patents (US, WO, EP, 1976+) from selected primary IPC classes.
  - For full usability set up an individual account for access on and off campus. Java and JRE plugins may be required.
  - Permitted Uses

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Google Scholar, PubChem, Reaxys, SciFinder-n, Web of Science Core Collection…

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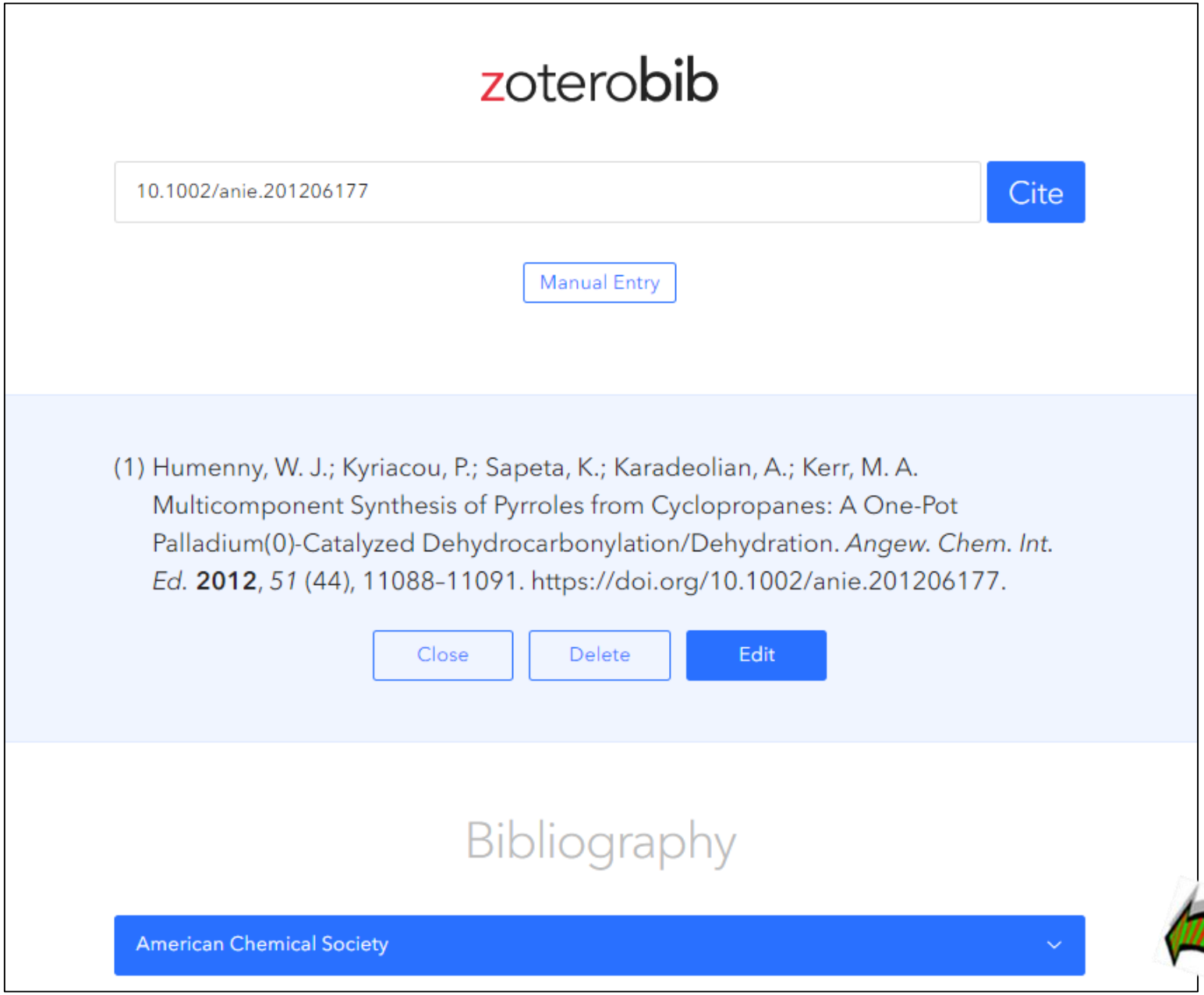
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10.1002/anie.201206177
Cite
Manual Entry
(1) Humenny, W. J.; Kyriacou, P.; Sapeta, K.; Karadeolian, A.; Kerr, M. A. Multicomponent Synthesis of Pyrroles from Cyclopropanes: A One-Pot Palladium(0)-Catalyzed Dehydrocarbonylation/Dehydration. *Angew. Chem. Int. Ed.* **2012**, *51* (44), 11088–11091. https://doi.org/10.1002/anie.201206177.
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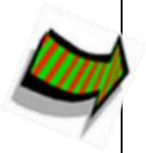

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   _____

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   _____

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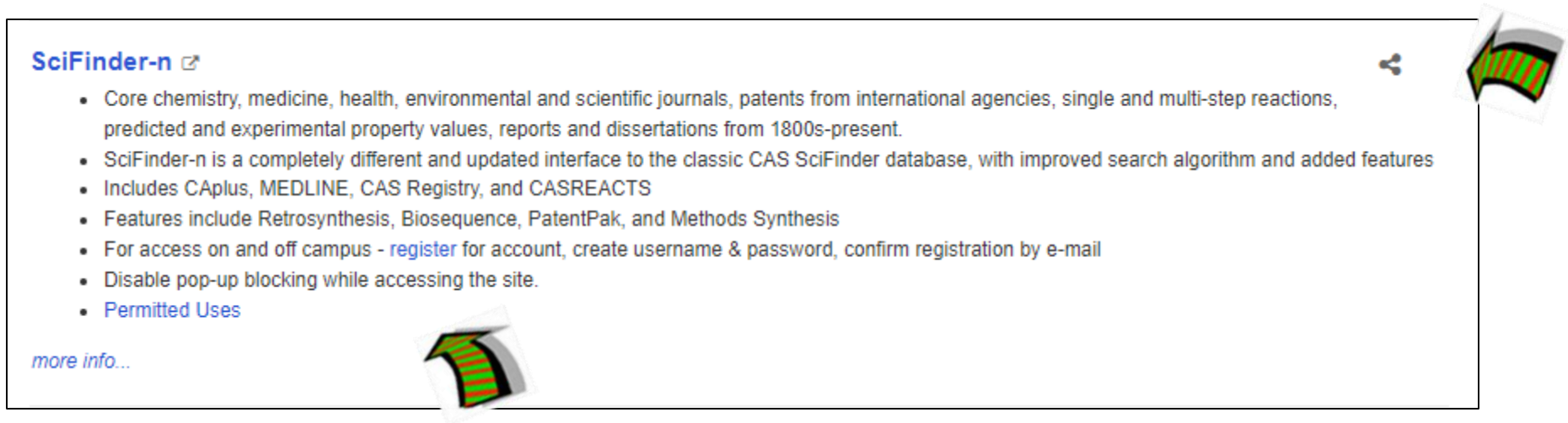
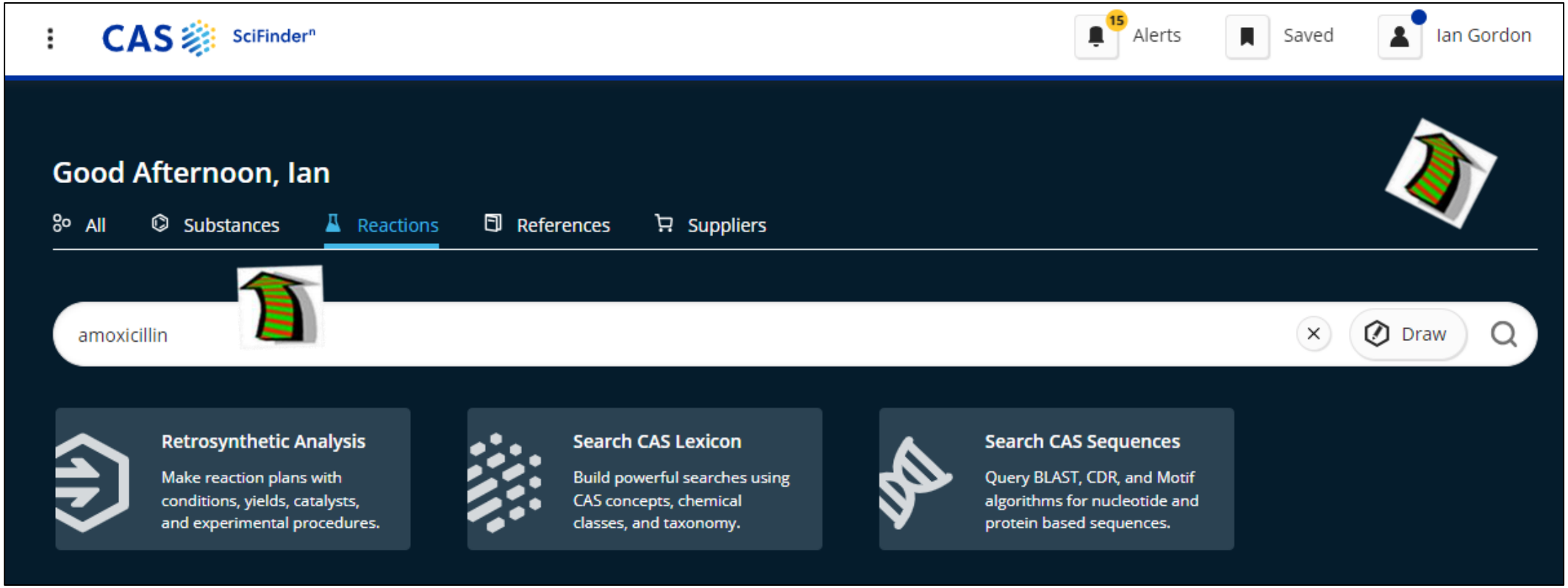
   How many retrieved reactions searching your drug as a drawn structure? ____
   How many retrieved Results when searching your drug name and the keyword prepar* in Reference titles? ____
   How many of these references are patents? Document Type = Patent? ____

   Sort citations by relevance, yield, number of steps, date, relevance… Select the most recent or one of the most interesting patents, check out the citation, indexing, click on PatentPak and Full Text, and cite it below using ACS Citation (with title) style:

   _____

https://researchguides.library.brocku.ca/database-scifinder


SciFinder-n
Core chemistry, medicine, health, environmental and scientific journals, patents from international agencies, single and multi-step reactions, predicted and experimental property values, reports and dissertations from 1800s-present.
SciFinder-n is a completely different and updated interface to the classic CAS SciFinder database, with improved search algorithm and added features
Includes CAplus, MEDLINE, CAS Registry, and CASREACTS
Features include Retrosynthesis, Biosequence, PatentPak, and Methods Synthesis
For access on and off campus - register for account, create username & password, confirm registration by e-mail
Disable pop-up blocking while accessing the site.
Permitted Uses
more info...


CAS SciFinder
15
Alerts
Saved
Ian Gordon
Good Afternoon, Ian
All
Substances
Reactions
References
Suppliers
amoxicillin
Draw
Retrosynthetic Analysis
Make reaction plans with conditions, yields, catalysts, and experimental procedures.
Search CAS Lexicon
Build powerful searches using CAS concepts, chemical classes, and taxonomy.
Search CAS Sequences
Query BLAST, CDR, and Motif algorithms for nucleotide and protein based sequences.

CAS SciFinder^n | Substances | amoxicillin | Edit

Return to Home

Substances search for "amoxicillin" + drawn structure

References | Reactions | Suppliers | Save and Alert

Structure Match

- As Drawn (1)
- Substructure (1)
- Similarity (1)

Analyze Structure Precision

Chemscape Analysis

Visually explore structure similarity with a powerful new tool.
Learn more about Chemscape.

Create Chemscape Analysis

Filter Behavior

Filter by | Exclude

Search Within Results

Reaction Role

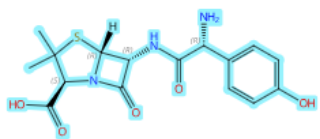
- [x] Product (1)
- [ ] Reactant (1)
- [ ] Reagent (1)

Filtering: Reaction Role: **Product** | Stereochemistry: **Absolute Stereo Match** | Clear All Filters

1 Result | View: Partial

1

26787-78-0



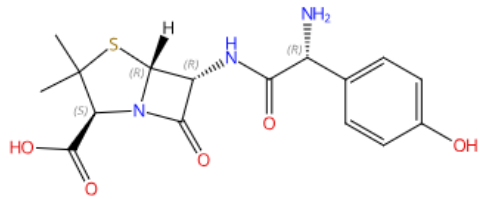
Absolute stereochemistry shown

$C_{16}H_{19}N_3O_5S$
Amoxicillin

34K References | 476 Reactions | 69 Suppliers

CAS Registry Number: 26787-78-0

34K | 475 | 69 | Save



Absolute stereochemistry shown

$C_{16}H_{19}N_3O_5S$

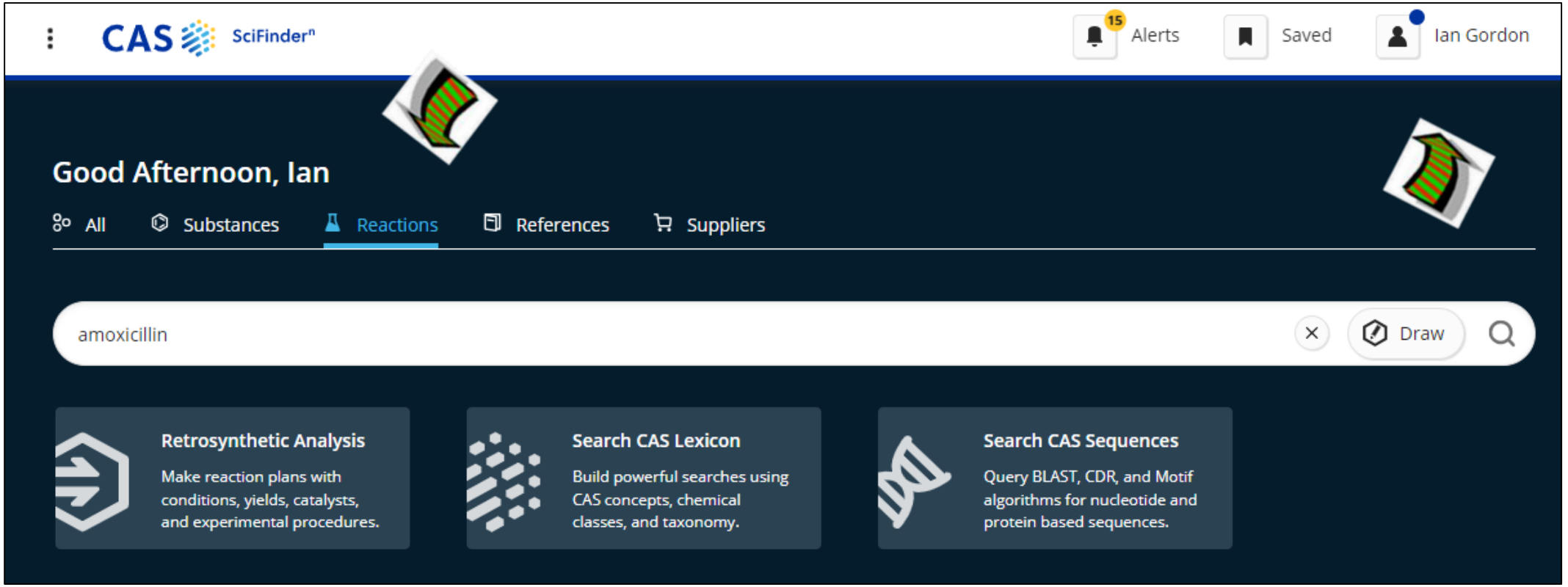
4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[(2*R*)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-, (2*S*,5*R*,6*R*)- (ACI)

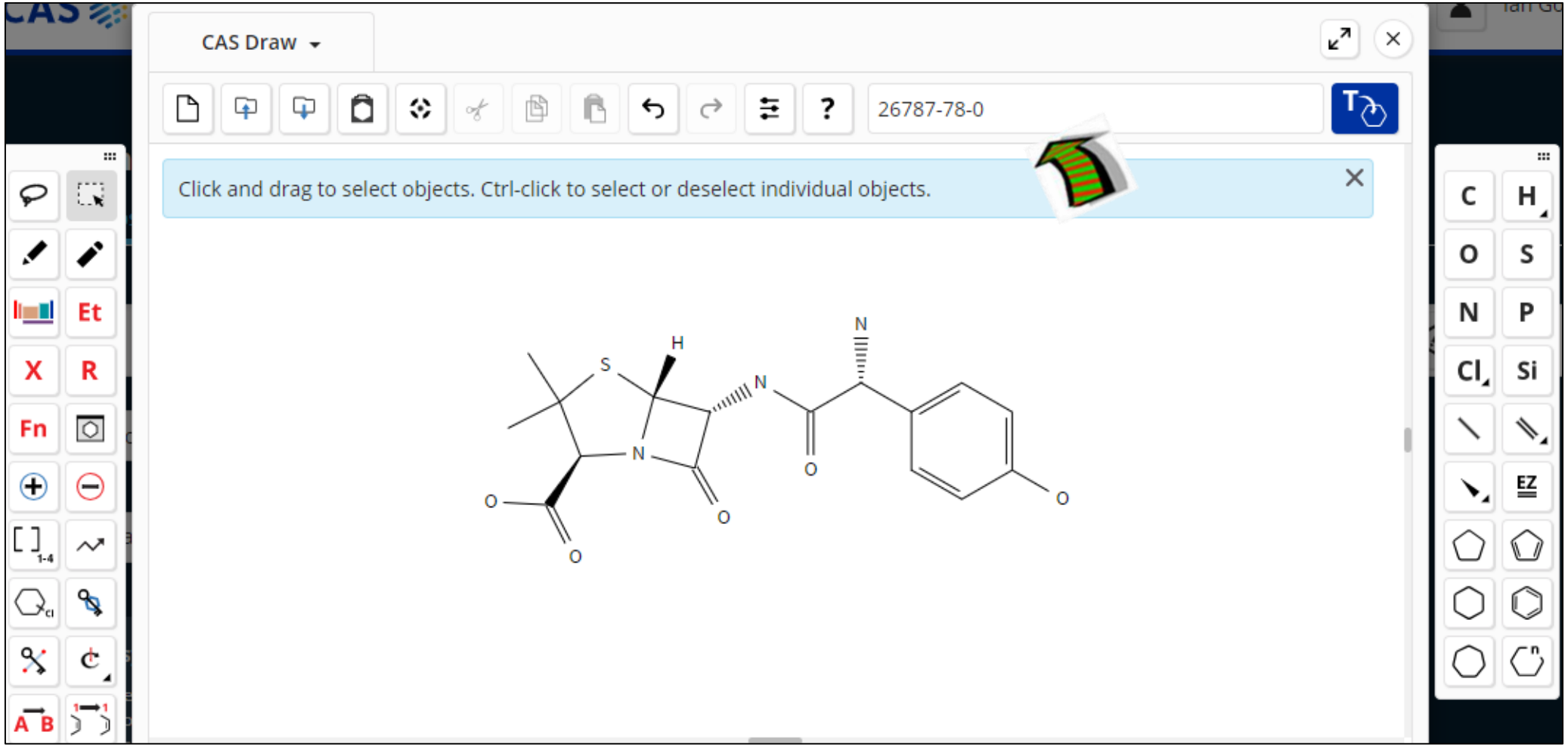
Key Physical Properties	Value	Condition
Molecular Weight	365.41	-
Melting Point (Experimental)	140 °C	-
Boiling Point (Predicted)	743.2±60.0 °C	Press: 760 Torr
Density (Predicted)	1.54±0.1 g/cm^3	Temp: 20 °C; Press: 760 Torr
pKa (Predicted)	2.44±0.50	Most Acidic Temp: 25 °C

Experimental Properties | Spectra

Expand All | Collapse All

- Other Names and Identifiers
- Experimental Properties
- Experimental Spectra
- Predicted Properties
- Predicted Spectra
- Bioactivity Indicators
- Target Indicators
- Regulatory Information
- GHS Hazard Statements
- Additional Details


CAS SciFinder
15
Alerts
Saved
Ian Gordon
Good Afternoon, Ian
All
Substances
Reactions
References
Suppliers
amoxicillin
Draw
Retrosynthetic Analysis
Make reaction plans with conditions, yields, catalysts, and experimental procedures.
Search CAS Lexicon
Build powerful searches using CAS concepts, chemical classes, and taxonomy.
Search CAS Sequences
Query BLAST, CDR, and Motif algorithms for nucleotide and protein based sequences.


CAS Draw
26787-78-0
Click and drag to select objects. Ctrl-click to select or deselect individual objects.
Et
X
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S
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O

Substances search for "amoxicillin"

References ▾ | Reactions ▾ | Suppliers ▾ | Save and Alert

Filter Behavior

Filter by | Exclude

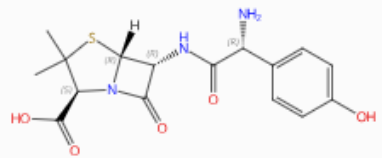
- Search Within Results
- Reaction Role
  - Product (1)
  - Reactant (1)
  - Reagent (1)
  - Catalyst (1)
- Reference Role
  - Adverse Effect (1)
  - Agricultural Use (1)
  - Analyte (1)
  - Analytical Matrix (1)
  - Analytical Reagent Use (1)
  - View All
- Commercial Availability
  - Available (1)
- Number of Components
- Molecular Weight
- LogP
- Stereochemistry

1 Result

View: Partial ▾

1

26787-78-0



Absolute stereochemistry shown

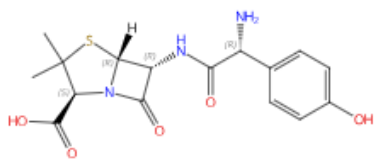
$C_{16}H_{19}N_3O_5S$

Amoxicillin

34K References | 475 Reactions | 69 Suppliers

1

26787-78-0



Absolute stereochemistry shown

$C_{16}H_{19}N_3O_5S$

Amoxicillin

34K References | 475 Reactions | 69 Suppliers

Key Physical Properties	Value	Condition
Molecular Weight	365.41	-
Melting Point (Experimental)	140 °C	-
Boiling Point (Predicted)	743.2±60.0 °C	Press: 760 Torr
Density (Predicted)	1.54±0.1 g/cm^3	Temp: 20 °C; Press: 760 Torr
pKa (Predicted)	2.44±0.50	Most Acidic Temp: 25 °C

Experimental Properties | Spectra

Reactions from Substances

References ▾ | Save and Alert

Filter Behavior

Filter by | Exclude

Search Within Results

Substance Role

- [x] Product (189)
- [ ] Reactant (289)
- [ ] Reagent (1)
- [ ] Catalyst (2)

Yield

- [ ] 90-100% (9)
- [ ] 80-89% (6)
- [ ] 70-79% (2)
- [ ] 50-69% (4)
- [ ] 30-49% (2)

View All

Number of Steps

- [ ] 1 (69)
- [ ] 2 (13)
- [ ] 3 (3)
- [ ] 4 (1)

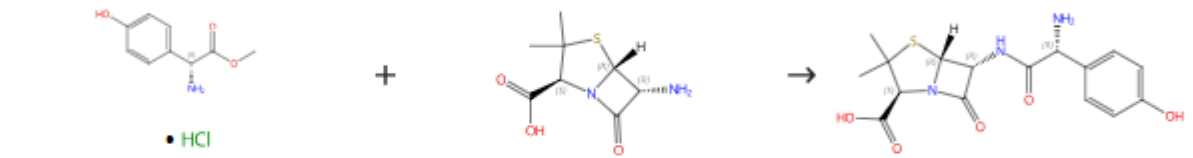
Non-Participating Functional Groups

Filtering: Substance Role: Product ×

Clear All Filters

189 Results | Group: By Scheme ▾ | Sort: Publication Date: Newest ▾ | View: Expanded ▾

Scheme 1 (4 Reactions) Steps: 1 Yield: 83-94% •••



Absolute stereochemistry shown, Rotation (-) | Absolute stereochemistry shown, Rotation (+) | Absolute stereochemistry shown

Suppliers (58) | Suppliers (107) | Suppliers (69)

31-614-CAS-36057352 Steps: 1 Yield: 94% •••

1.1 Catalysts: Penicillin amidase; pH 6.5 - 6.9

Method for preparing amoxicillin crystal

By: Miao, Ruichun; et al
China, CN115490706 A 2022-12-20

PatentPak ▾ | Full Text ▾

31-368-CAS-15581463 Steps: 1 Yield: 94% •••

1.1 Reagents: Ammonium hydroxide
Catalysts: Penicillin amidase
Solvents: Water; pH 6.2 - 6.4, 19 - 21 °C
1.2 Reagents: Hydrochloric acid
Solvents: Water; pH 1.17
1.3 Reagents: Ammonium hydroxide
Solvents: Water; pH 5.1

A method for recycling amoxicillin mother liquor

By: Chen, Yingxin; et al
China, CN105567777 A 2016-05-11

PatentPak ▾ | Full Text ▾

Filter Behavior

Filter by | Exclude

Search Within Results

Substance Role

- [x] Product (189)
- [ ] Reactant (289)
- [ ] Reagent (1)
- [ ] Catalyst (2)

Yield

Number of Steps

Non-Participating Functional Groups

Reaction Mapping

Reaction Scale

Experimental Protocols

Reaction Type

Stereochemistry

Reagent

Catalyst

Solvent

Commercial Availability

Reaction Notes

Source Reference

Document Type

Language

Publication Year

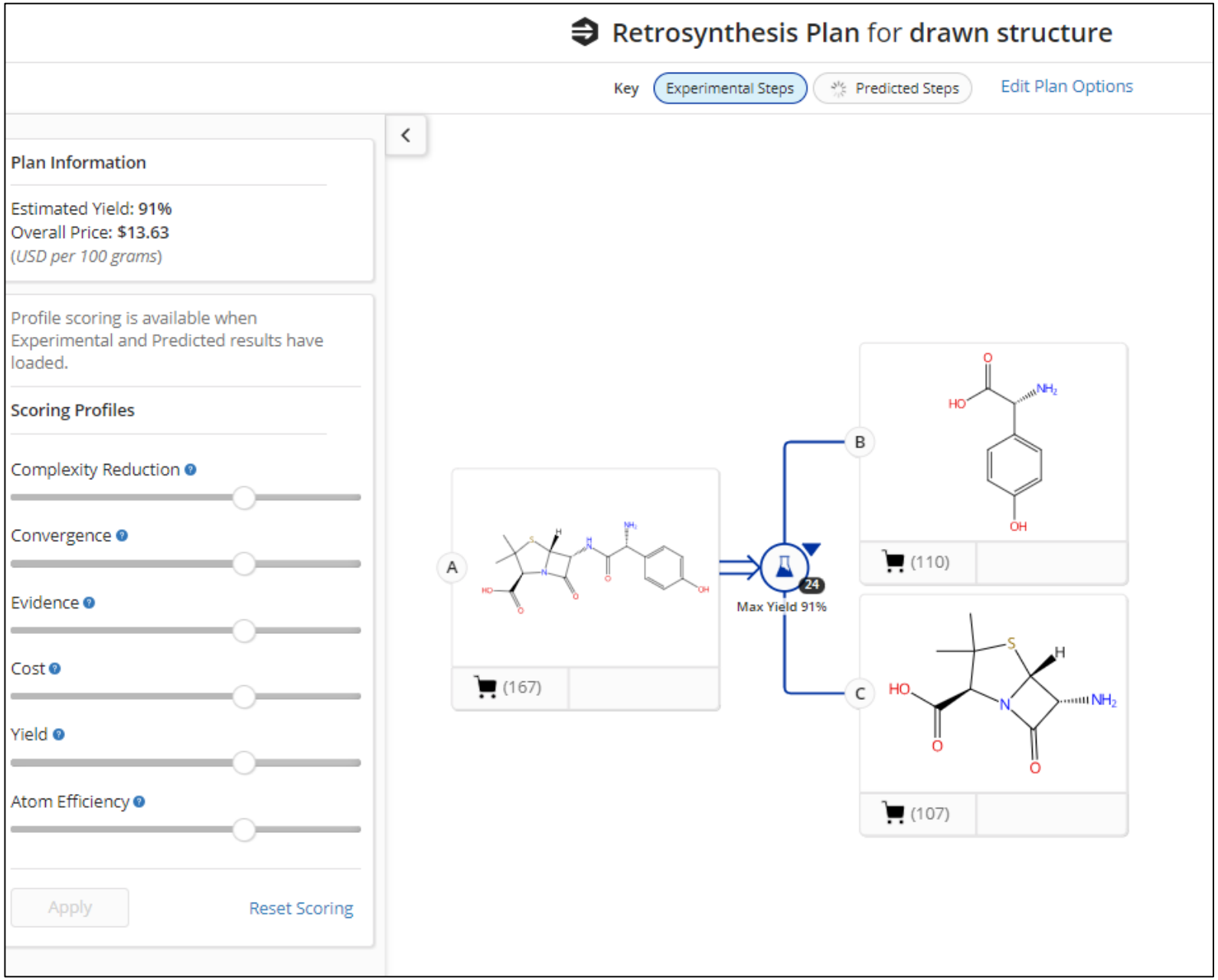
Organization

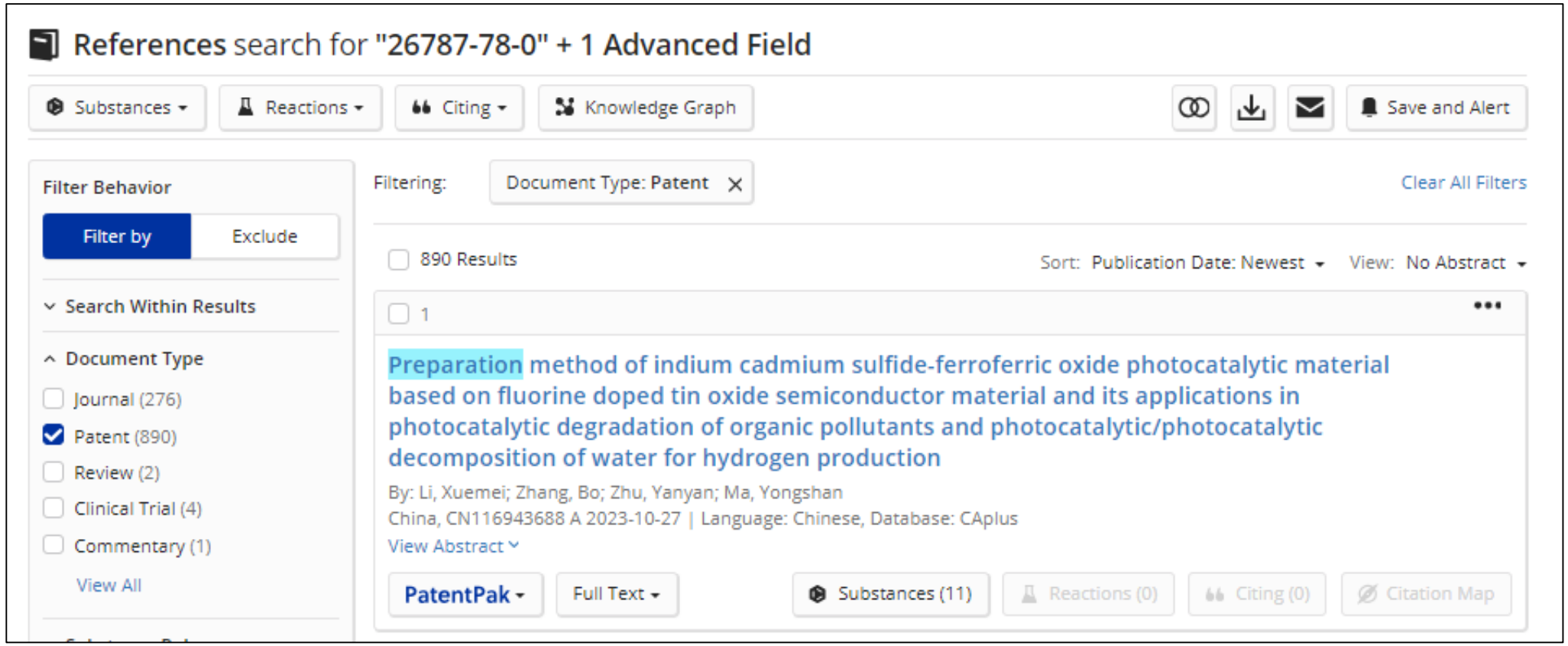
Publication Name

CA Section

Filter Content Report

Download filter data from this result set.


Retrosynthesis Plan for drawn structure
Key
Experimental Steps
Predicted Steps
Edit Plan Options
Plan Information
Estimated Yield: 91%
Overall Price: $13.63
(USD per 100 grams)
Profile scoring is available when Experimental and Predicted results have loaded.
Scoring Profiles
Complexity Reduction
Convergence
Evidence
Cost
Yield
Atom Efficiency
Apply
Reset Scoring
A
(167)
24
Max Yield 91%
B
(110)
C
(107)


References search for "26787-78-0" + 1 Advanced Field
Substances
Reactions
Citing
Knowledge Graph
Save and Alert
Filter Behavior
Filter by
Exclude
Search Within Results
Document Type
Journal (276)
Patent (890)
Review (2)
Clinical Trial (4)
Commentary (1)
View All
Filtering:
Document Type: Patent
Clear All Filters
890 Results
Sort: Publication Date: Newest
View: No Abstract
1
Preparation method of indium cadmium sulfide-ferroferric oxide photocatalytic material based on fluorine doped tin oxide semiconductor material and its applications in photocatalytic degradation of organic pollutants and photocatalytic/photocatalytic decomposition of water for hydrogen production
By: Li, Xuemei; Zhang, Bo; Zhu, Yanyan; Ma, Yongshan
China, CN116943688 A 2023-10-27 | Language: Chinese, Database: CAplus
View Abstract
PatentPak
Full Text
Substances (11)
Reactions (0)
Citing (0)
Citation Map

References search for "amoxicillin" + 1 Advanced Field
Substances
Reactions
Citing
Knowledge Graph
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Filter Behavior
Filter by
Exclude
Search Within Results
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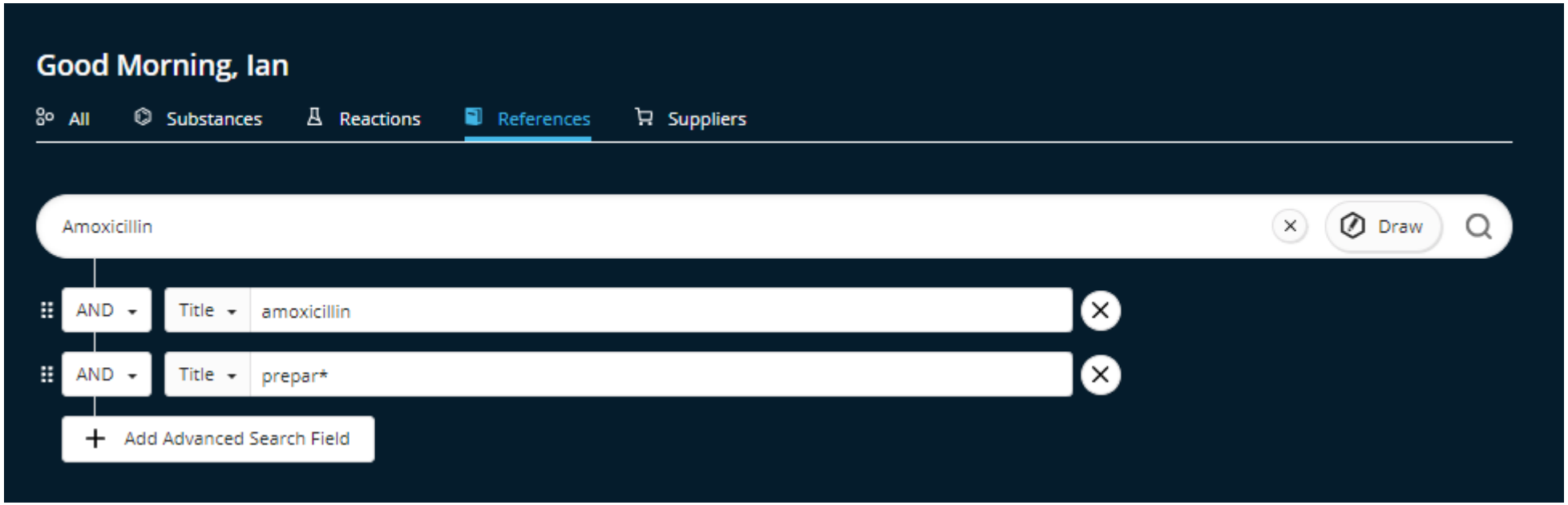
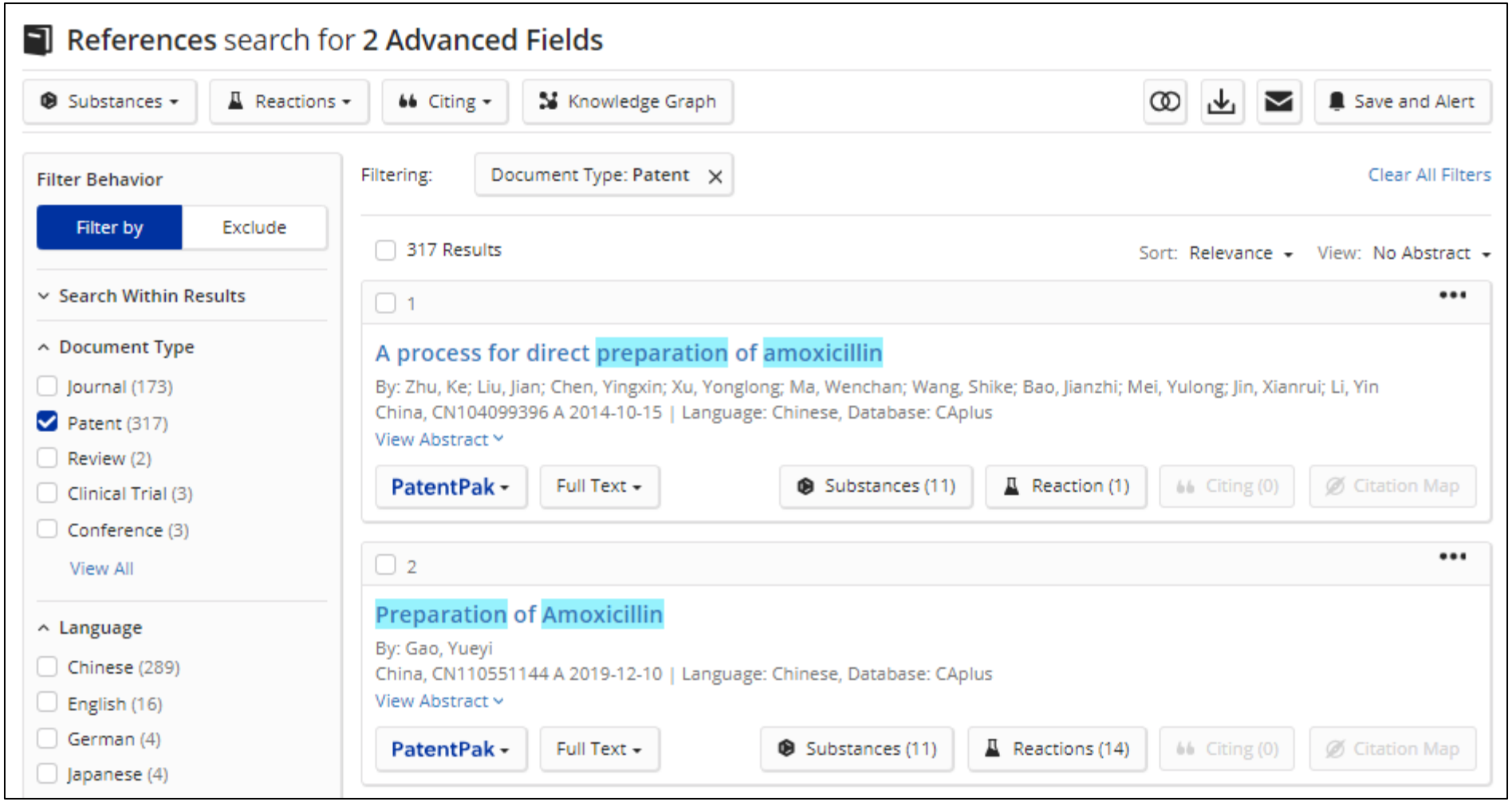
Patent (999)
Review (4)
Clinical Trial (6)
Commentary (1)
View All
Filtering:
Document Type: Patent
Clear All Filters
999 Results
Sort: Publication Date: Newest
View: No Abstract
1
A method for preparing ternary visible light-responsive controllable drug release material based on double-layer titanium dioxide nanotube array
By: Li, Ping; Jiang, Huaiyuan; Liu, Ruizhen; Lv, Renliang; Gu, Shuangxi; Xu, Caili; Yin, Jianfei; Xu, Zhengrui; Chen, Xiaoyu
China, CN117085145 A 2023-11-21 | Language: Chinese, Database: CAplus
View Abstract
PatentPak
Full Text
Substances (0)
Reactions (0)
Citing (0)
Citation Map


Good Morning, Ian
All
Substances
Reactions
References
Suppliers
Amoxicillin
Draw
AND
Title
amoxicillin
AND
Title
prepar*
Add Advanced Search Field


References search for 2 Advanced Fields
Substances
Reactions
Citing
Knowledge Graph
Save and Alert
Filter Behavior
Filter by
Exclude
Search Within Results
Document Type
Journal (173)
Patent (317)
Review (2)
Clinical Trial (3)
Conference (3)
View All
Language
Chinese (289)
English (16)
German (4)
Japanese (4)
Filtering:
Document Type: Patent
Clear All Filters
317 Results
Sort: Relevance
View: No Abstract
1
A process for direct preparation of amoxicillin
By: Zhu, Ke; Liu, Jian; Chen, Yingxin; Xu, Yonglong; Ma, Wenchan; Wang, Shike; Bao, Jianzhi; Mei, Yulong; Jin, Xianrui; Li, Yin
China, CN104099396 A 2014-10-15 | Language: Chinese, Database: CAplus
View Abstract
PatentPak
Full Text
Substances (11)
Reaction (1)
Citing (0)
Citation Map
2
Preparation of Amoxicillin
By: Gao, Yueyi
China, CN110551144 A 2019-12-10 | Language: Chinese, Database: CAplus
View Abstract
PatentPak
Full Text
Substances (11)
Reactions (14)
Citing (0)
Citation Map

5. Go to PubChem, find your drug, check out all contents, completing the following:

   What is the PubChem CID for your drug? ___

   What is the next highest MeSH and Thesaurus Tree classification names for your drug?

   _____

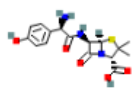
PubChem About Docs Submit Contact

SEARCH FOR

amoxicillin

Treating this as a text search.

BEST MATCH



amoxicillin; Amoxycillin; 26787-78-0; Amoxicillin anhydrous; Amoxicilline; p-Hydroxyampicillin; Amopenixin; Amolin; ...

Compound CID: 33613

MF: $C_{16}H_{19}N_3O_5S$ **MW:** 365.4g/mol

IUPAC Name: (2S,5R,6R)-6-[[(2R)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid

Isomeric SMILES: CC1([C@@H](N2[C@H](S1)[C@@H](C2=O)NC(=O)[C@@H](C3=CC=C(C=C3)O)N)C(=O)O)C

InChIKey: LSQZJLSUYDQPKJ-NJBDSQKTSA-N

InChI: InChI=1S/C16H19N3O5S/c1-16(2)11(15(23)24)19-13(22)10(14(19)25-16)18-12(21)9(17)7-3-5-8(20)6-4-7/h3-6,9-11,14,20H,17H2,1-2H3,(H,18,21)(H,23,24)/t9-,10-,11+,14-/m1/s1

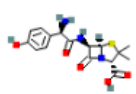
Create Date: 2005-06-24

Summary Similar Structures Search Related Records PubMed (MeSH Keyword)

Compounds (80)	Substances (671)	BioAssays (1,907)	Literature (24,341)	Patents (1,012)

Searching chemical names and synonyms including IUPAC names and InChIKeys across the compound collection. Note that annotations text from compound summary pages is not searched. Read More...

80 results Filters SORT BY Relevance



amoxicillin; Amoxycillin; 26787-78-0; Amoxicillin anhydrous; Amoxicilline; ...

Compound CID: 33613

MF: $C_{16}H_{19}N_3O_5S$ **MW:** 365.4g/mol

IUPAC Name: (2S,5R,6R)-6-[[(2R)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid

Isomeric SMILES: CC1([C@@H](N2[C@H](S1)[C@@H](C2=O)NC(=O)[C@@H](C3=CC=C(C=C3)O)N)C(=O)O)C

InChIKey: LSQZJLSUYDQPKJ-NJBDSQKTSA-N

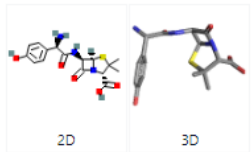
InChI: InChI=1S/C16H19N3O5S/c1-16(2)11(15(23)24)19-13(22)10(14(19)25-16)18-12(21)9(17)7-3-5-8(20)6-4-7/h3-6,9-11,14,20H,17H2,1-2H3,(H,18,21)(H,23,24)/t9-,10-,11+,14-/m1/s1

Create Date: 2005-06-24

PubChem About Docs Submit Contact Search PubChem

COMPOUND SUMMARY

Amoxicillin

PubChem CID	33613
Structure	 2D 3D
Chemical Safety	Irritant Health Hazard Laboratory Chemical Safety Summary (LCSS) Datasheet
Molecular Formula	$C_{16}H_{19}N_3O_5S$
Synonyms	amoxicillin Amoxycillin 26787-78-0 Amoxicillin anhydrous Amoxicilline View More...
Molecular Weight	365.4 g/mol *Computed by PubChem 2.2 (PubChem release 2021.10.14)*

Cite Download

CONTENTS

Title and Summary
1 Structures
2 Names and Identifiers
3 Chemical and Physical Properties
4 Spectral Information
5 Related Records
6 Chemical Vendors
7 Drug and Medication Information
8 Food Additives and Ingredients
9 Pharmacology and Biochemistry
10 Use and Manufacturing
11 Identification
12 Safety and Hazards
13 Toxicity
14 Associated Disorders and Diseases
15 Literature
16 Patents
17 Interactions and Pathways
18 Biological Test Results
19 Taxonomy
20 Classification
21 Information Sources

20 Classification

20.1 MeSH Tree

1 item — View in Classification Browser

MeSH Tree > Chemicals and Drugs Category > Organic Chemicals > Sulfur Compounds > beta-Lactams > Penicillins > Penicillin G > Ampicillin

Amoxicillin

A broad-spectrum semisynthetic antibiotic similar to AMPICILLIN except that its resistance to gastric acid permits higher serum levels with oral administration.

▸ Medical Subject Headings (MeSH)

20.2 NCI Thesaurus Tree

2 items — View in Classification Browser

NCI Thesaurus Tree > Drug, Food, Chemical or Biomedical Material > Pharmacologic Substance > Anti-Infective Agent > Antibiotic > Beta-Lactam Antibiotic > Penicillin Antibiotic

Amoxicillin Anhydrous

The anhydrous form of a broad-spectrum, semisynthetic aminopenicillin antibiotic with bactericidal activity. Amoxicillin binds to and inactivates penicillin-binding proteins (PBPs) located on the inner membrane of the bacterial cell wall. Inactivation of PBPs interferes with the cross-linkage of peptidoglycan chains necessary for bacterial cell wall strength and rigidity. This interrupts bacterial cell wall synthesis and results in the weakening of the bacterial cell wall and causes cell lysis.

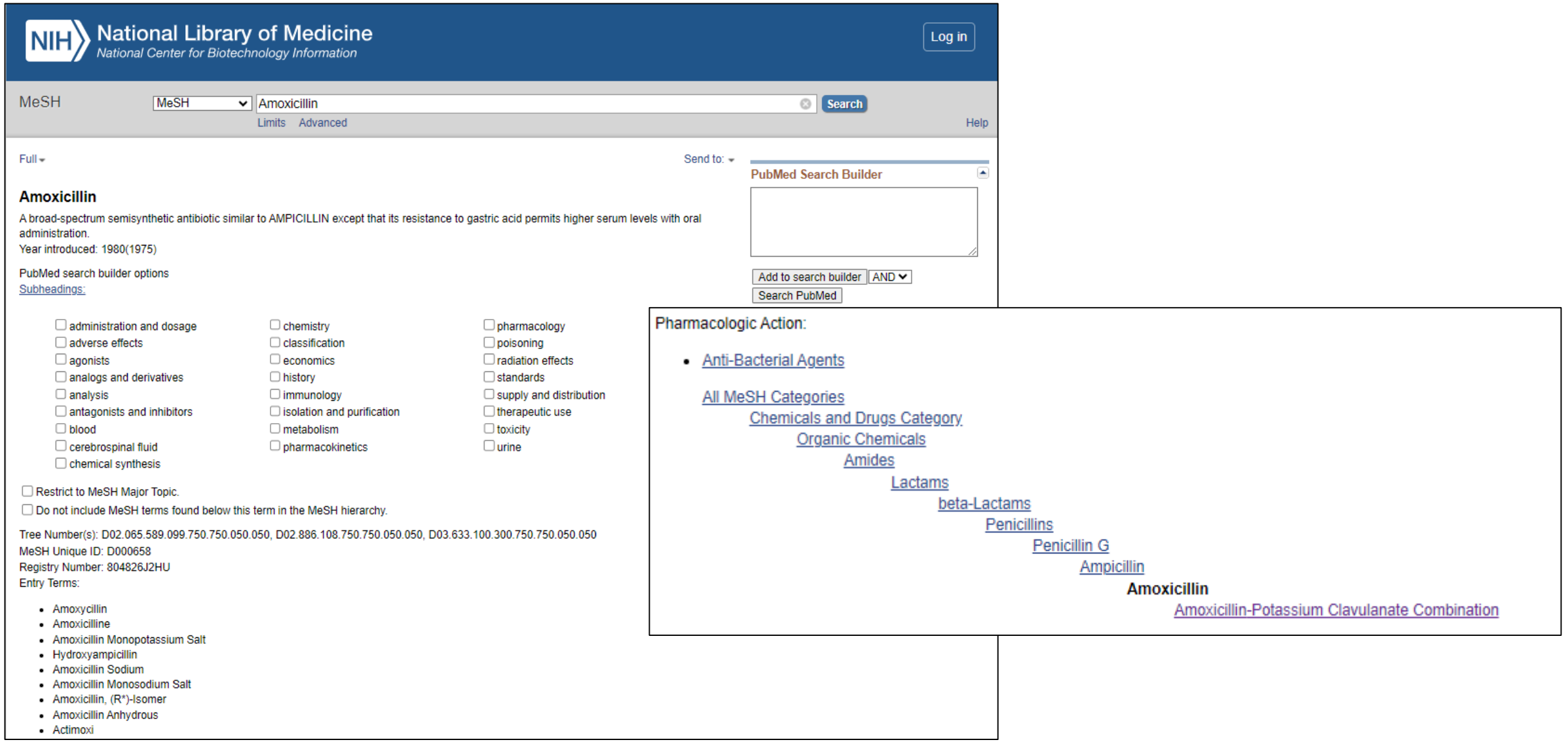
NCI Thesaurus Tree > Drug, Food, Chemical or Biomedical Material > Pharmacologic Substance > Anti-Infective Agent > Antibiotic > Beta-Lactam Antibiotic > Penicillin Antibiotic

Amoxicillin

A broad-spectrum, semisynthetic aminopenicillin antibiotic with bactericidal activity. Amoxicillin binds to and inactivates penicillin-binding protein (PBP) 1A located on the inner membrane of the bacterial cell wall. Inactivation of PBPs interferes with the cross-linkage of peptidoglycan chains necessary for bacterial cell wall strength and rigidity. This interrupts bacterial cell wall synthesis and results in the weakening of the bacterial cell wall and causes cell lysis.

▸ NCI Thesaurus (NCIt)

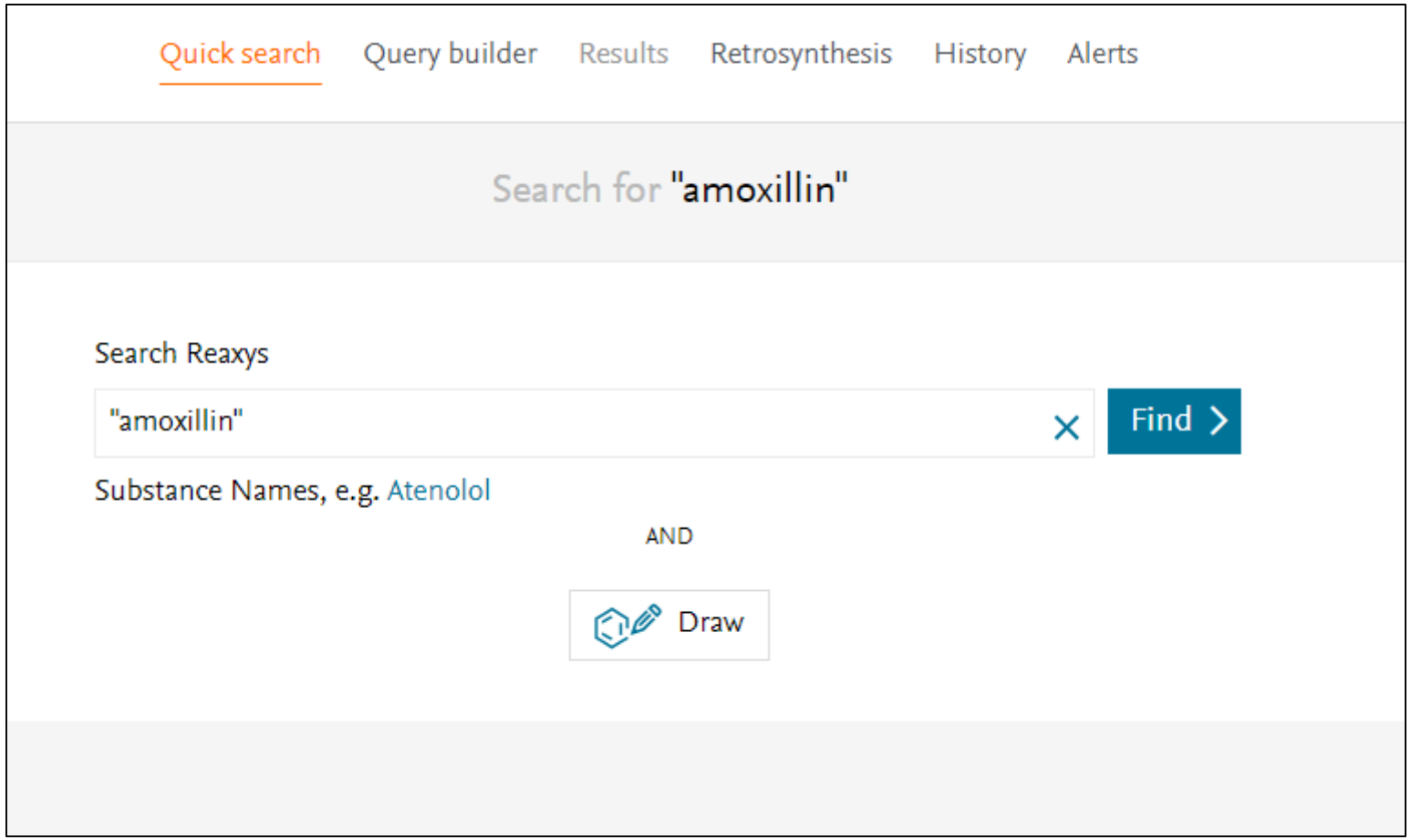
https://www.ncbi.nlm.nih.gov/mesh/68000658



6. Go to the Reaxys database (no registration needed). Do a "Quick search" which is the default setting. Search for your drug, view the most appropriate entry, indicate:

   What is the Reaxys ID number for your drug? ___
   Number of Reaxys preparations ___, documents ___, and reactions ___
   Click on the Retrosynthesis tab at the top of the Reaxys search page, look up your compound and run your synthesis which takes all reactions, variant compounds and then looks to produce an algorithmically AI search reaction tree complete with experimental procedures when available for your benefit. View the future of synthetic organic chemistry that will soon AI data to run biological sequences, target groups, steps, reactions… all linked to article and patent citations.
   How many published retrosynthesis did Reaxys find? ___

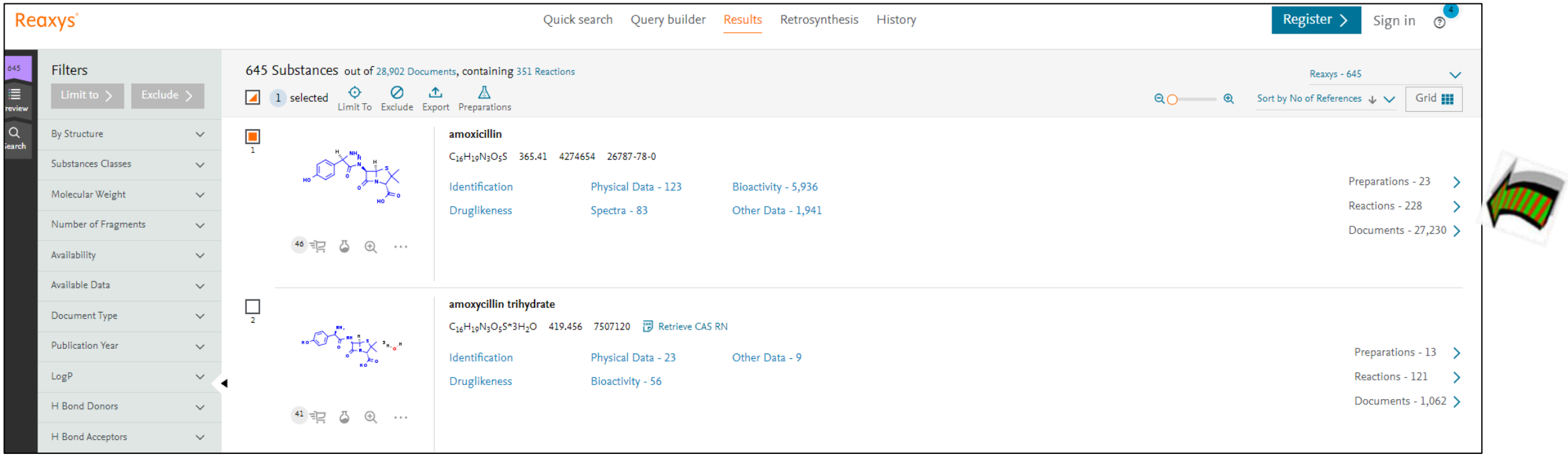
Reaxys®


Quick search
Query builder
Results
Retrosynthesis
History
Alerts
Search for "amoxillin"
Search Reaxys
"amoxillin"
Find
Substance Names, e.g. Atenolol
AND
Draw

Results for **amoxicillin**

New Edit

645	Substances	Structure : as drawn Edit in Query Builder Create Alert	Preview Results	View Results
230,841	Documents	Structure : as drawn Titles, Abstracts, Keywords : "amoxicillin" Edit in Query Builder Create Alert	Preview Results	View Results
18	Commercial Substances	Structure : as drawn Edit in Query Builder Create Alert	Preview Results	View Results


Reaxys
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Exclude
By Structure
Substances Classes
Molecular Weight
Number of Fragments
Availability
Available Data
Document Type
Publication Year
LogP
H Bond Donors
H Bond Acceptors
645 Substances out of 28,902 Documents, containing 351 Reactions
1 selected
Limit To
Exclude
Export
Preparations
Reaxys - 645
Sort by No of References
Grid
amoxicillin
C16H19N3O5S 365.41 4274654 26787-78-0
Identification
Physical Data - 123
Bioactivity - 5,936
Druglikeness
Spectra - 83
Other Data - 1,941
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amoxycillin trihydrate
C16H19N3O5S*3H2O 419.456 7507120
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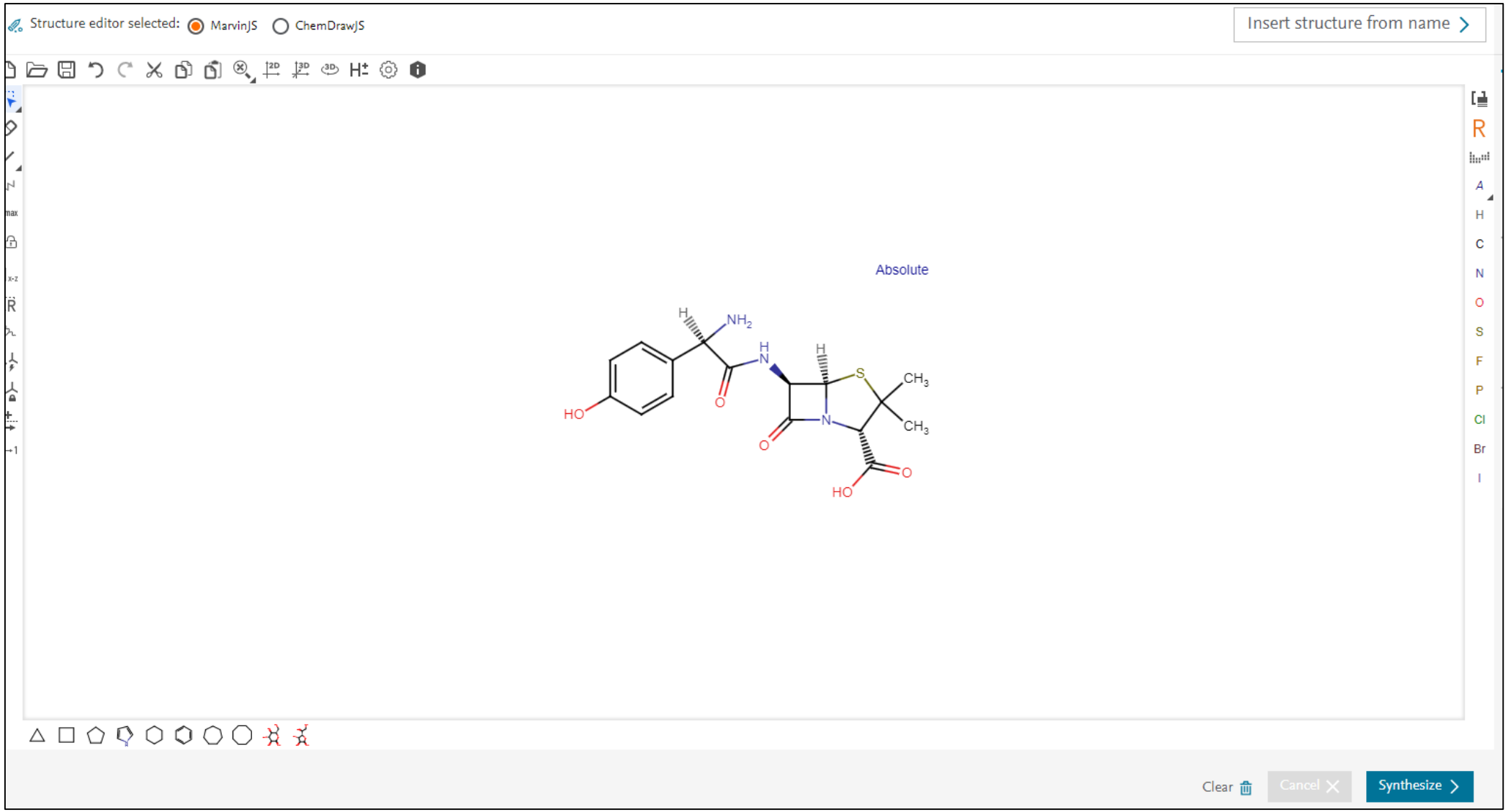
Identification
Physical Data - 23
Other Data - 9
Druglikeness
Bioactivity - 56
Preparations - 13
Reactions - 121
Documents - 1,062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MarvinJS
ChemDrawJS
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Absolute
H
NH2
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N
H
S
CH3
CH3
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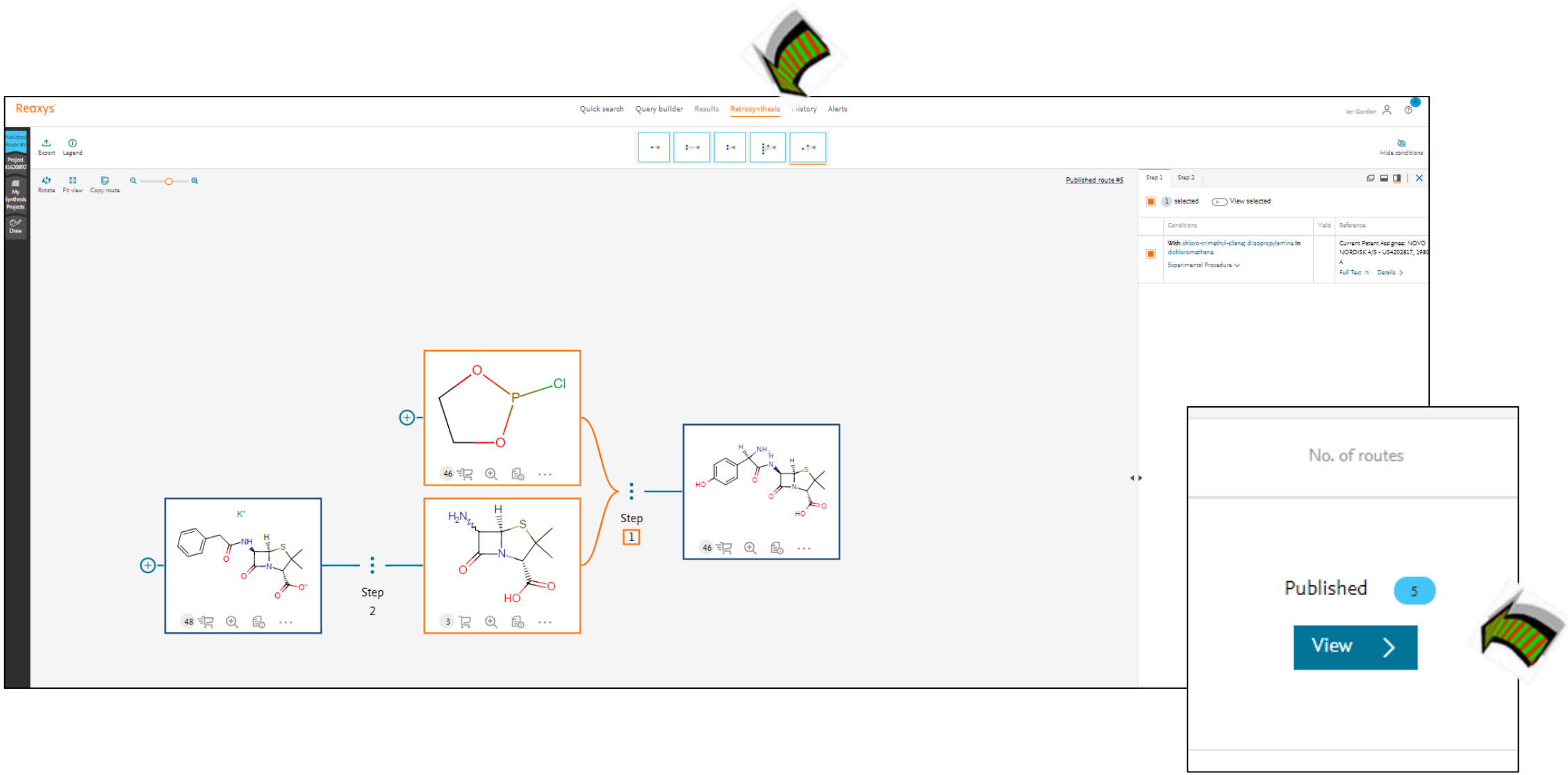
Synthesize


Reaxys
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Query builder
Results
Retrosynthesis
Alerts
Export
Legend
Hide conditions
Rotate
Fit view
Copy route
Published route #5
Step 1
Step 2
1 selected
View selected
Conditions
Yield
Reference
With chloro-trimethyl-silane; diisopropylamine in dichloromethane
Experimental Procedure
Full Text
Details
Step 2
Step 1
No. of routes
Published
5
View

7. Using Reaxys, click on new search, do a "Query builder" search this time which guides you through a search strategy one step at a time. Search for your drug (e.g. CAS no.), select "Search in: Reactions", filter/limit to "Yield", filter/limit to Document Type "article", sort by "Reaxys ranks" and pick one of the current or most interesting articles.

   What is this reaction yield ___% and include the citation using ACS Citation (with title) style.

   _____

Reaxys

172 Reactions out of 121 Documents, containing 351 Substances

0 selected | Limit To | Exclude | Export | Hide Conditions | Sort by Reaxys Ranking

228 Search

Filters

Limit to > | Exclude >

By Structure

Yield

- >95 - 100 4
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- >85 - 90 4
- >80 - 85 5
- >75 - 80 7
- >70 - 75 2
- >65 - 70 7

Filter by value | View more

Reagent/Catalyst

Solvent

Catalyst Classes

Solvent Classes

Product Availability

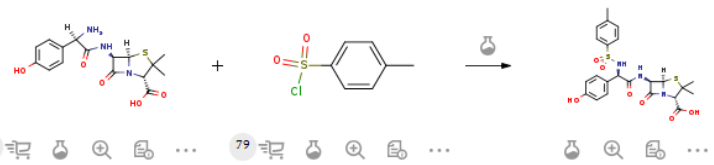
Reactant Availability

Reaction Classes

Document Type 1

- article 173
- patent 58

1

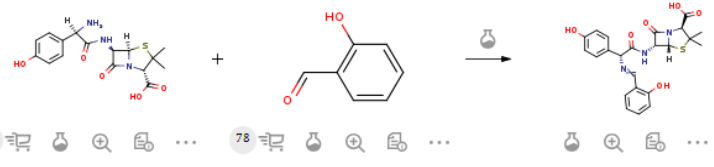


46 79

1 Conditions | Find Similar > | Reaction ID: 41701792

Conditions	Yield	Reference
Stage #1: amoxicillin; p-toluenesulfonyl chloride **In** water at 20°C; pH=8 - 9; **Stage #2: With** hydrogenchloride **In** water pH=2 - 3; Experimental Procedure	55%	Rehman, Hajira; Qadir, Abdul; Ali, Zulfiqar; Mahmood, Nasir; Zahra, Asmat; Hussain, Habib; Shahzady, Tanzeela Gulab [**Asian Journal of Chemistry, 2016**, vol. 28, # 2, p. 343 - 346] Full Text	Details >	Abstract >

2



46 78

2 Conditions | Find Similar > | Reaction ID: 41640047

Conditions	Yield	Reference
With sodium hydroxide **In** methanol; water for 2h; pH=7 - 8; Reflux; Experimental Procedure	81%	Reiss, Aurora; Samide, Adriana; Ciobanu, Georgeta; Dabuleanu, Irina [**Journal of the Chilean Chemical Society, 2015**, vol. 60, # 3, p. 3074 - 3079] Full Text	Cited 27 times	Details >	Abstract >
In ethanol for 3h; Inert atmosphere;	70%	Anacona; Loroño, Marcos; Marpa, Daniela; Ramos, Cesar; Celis, Freddy [**Applied Organometallic Chemistry, 2020**, vol. 34, # 9, art. no. E5755]

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Synthesis, spectroscopic characteristics and antibacterial study of some novel sulphonamides

Rehman, Hajira; Qadir, Abdul; Ali, Zulfiqar; Mahmood, Nasir; Zahra, Asmat; Hussain, Habib; Shahzady, Tanzeela Gulab [**Asian Journal of Chemistry, 2016**, vol. 28, # 2, p. 343 - 346]

Abstract Index Terms Substances 7 Reactions 3 Full Text

Abstract

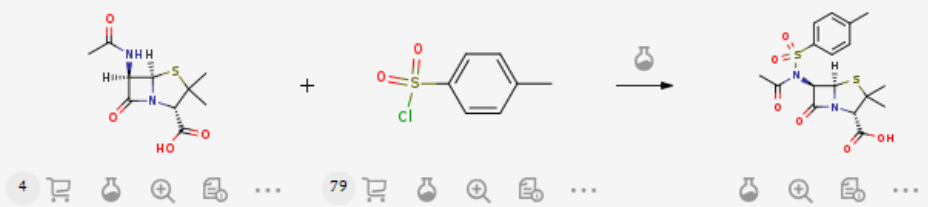
Main purpose of this study was to produce some novel sulfonamides from already existing antibiotics having-NH_2 group in their structure by their simple and low-cost conde were carried out in aqueous media at controlled pH (8-10) with good yield. Characterization of synthesized compounds were done by using FTIR, $_1$H NMR, ESI-MS and eleme cally important Gram-positive and Gram-negative bacterial strains using MIC method after observing optical density value by spectrophotometer at 600 nm. All compounds w while N-((2S,5R,6R)-2-formyl-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptanes-6-yl)-Ntosylacetamide (1) showed pronounced results having MIC value less than 6 µg/m

Index Terms

Author keyword: Antibiotics • P-Toluene sulfonyl chloride • Sulfonamides

Reaxys Index Terms: Chemical shifts • ESI (Electrospray ionisation) • HRMS (High resolution mass spectrometry) • IC50 • IR bands • MS spectrum • elemental analysis

Reactions



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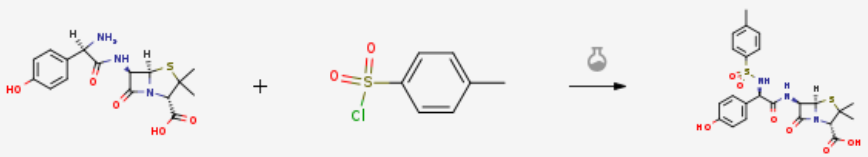
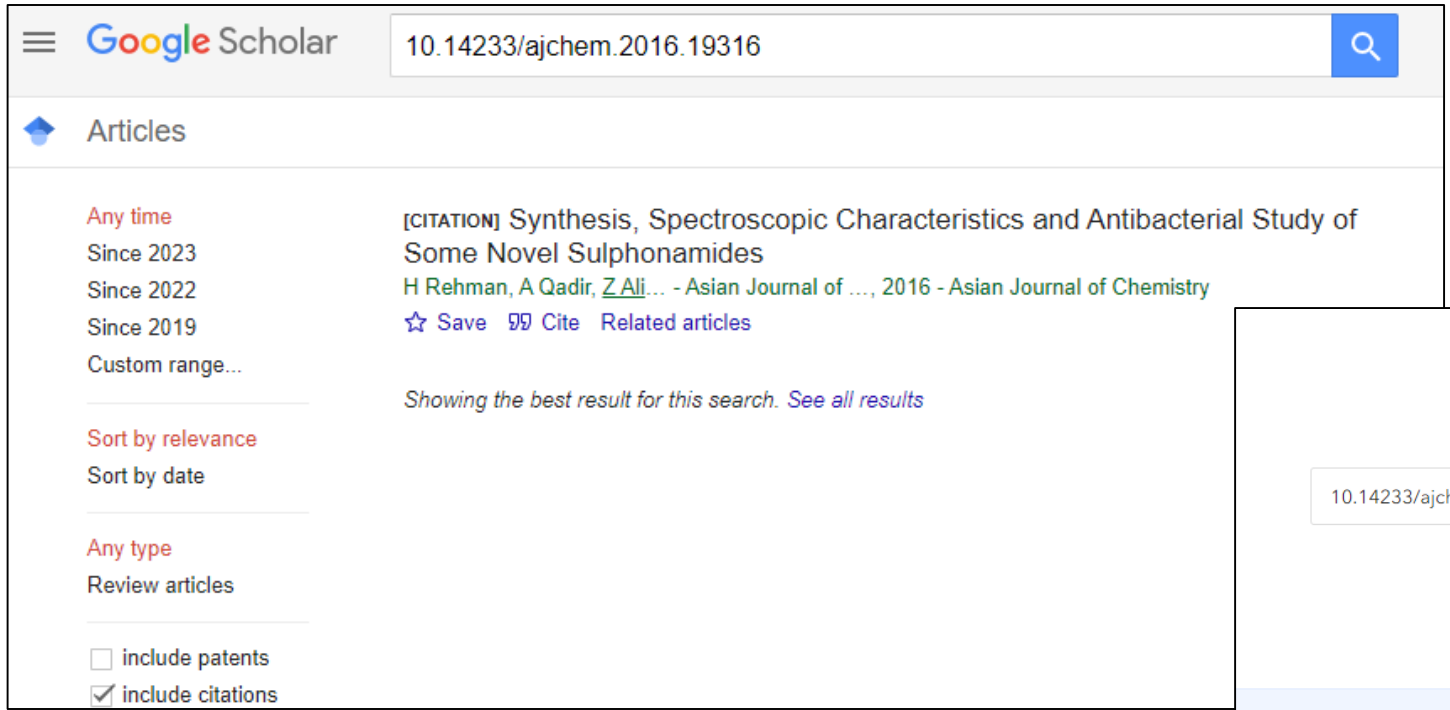
1 Conditions Find Similar Reaction ID: 41701791

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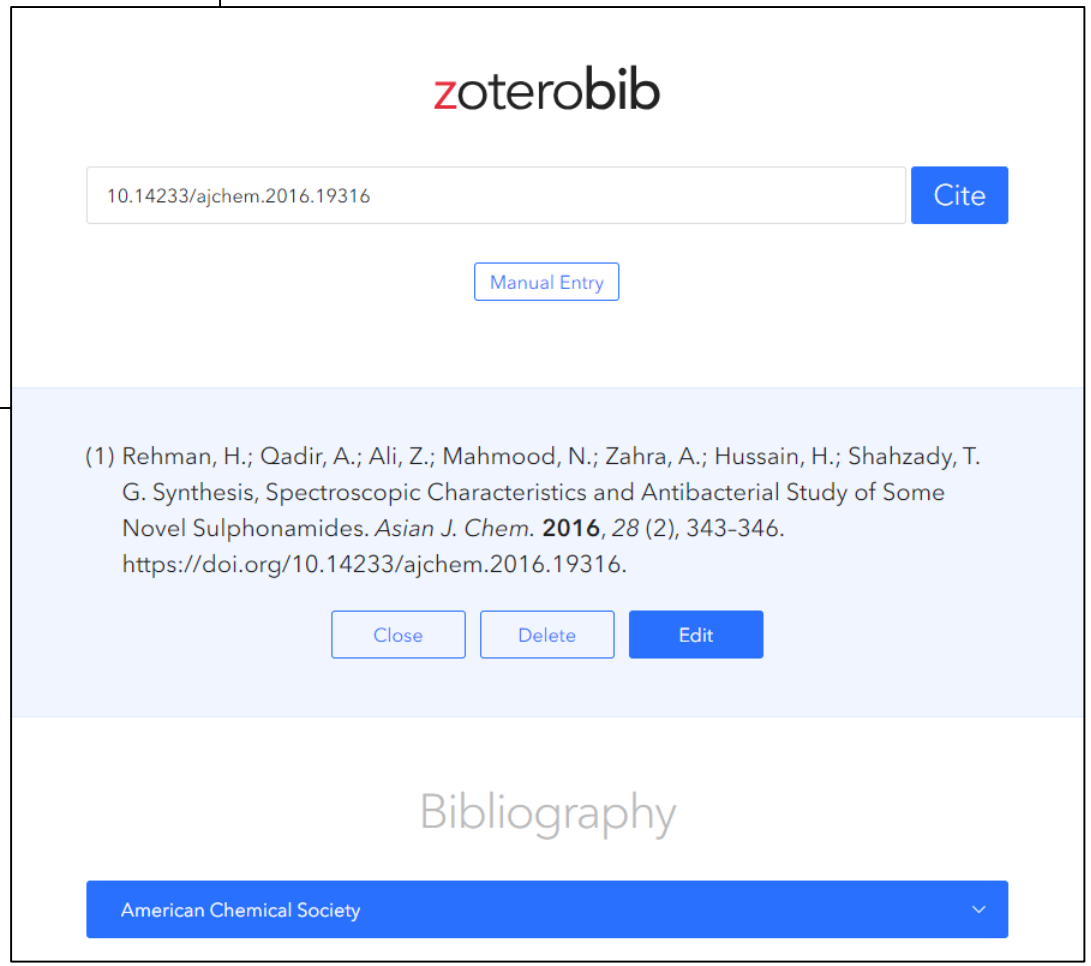
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(1) Rehman, H.; Qadir, A.; Ali, Z.; Mahmood, N.; Zahra, A.; Hussain, H.; Shahzady, T. G. Synthesis, Spectroscopic Characteristics and Antibacterial Study of Some Novel Sulphonamides. Asian J. Chem. 2016, 28 (2), 343-346. https://doi.org/10.14233/ajchem.2016.19316.
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Synthesis, Spectroscopic Characteristics and Antibacterial Study of Some Novel Sulphonamides

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Main purpose of this study was to produce some novel sulfonamides from already existing antibiotics having-NH_2 group in their structure by their simple and low-cost condensation reactions with *p*-toulene sulfonyl chloride. All reactions were carried out in aqueous media at controlled pH (8-10) with good yield. Characterization of synthesized compounds were done by using FTIR, ^{1}H NMR, ESI-MS and elemental analysis. Biological activity was evaluated against medically important Gram-positive and Gram-negative bacterial strains using MIC method after observing optical density value by spectrophotometer at 600 nm. All compounds were active against *E. coli* with MIC value less than 55 µg/mL, while N-((2S,5R,6R)-2-formyl-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptanes-6-yl)-N-tosylacetamide (**1**) showed pronounced results having MIC value less than 6 µg/mL for both strains.

Keywords: Sulfonamides, *p*-Toluene sulfonyl chloride, Antibiotics.

INTRODUCTION

The insist for new chemotherapeutic antibacterial leftovers attractive in branch of medicinal chemistry. The innovation of sulfonamides as antibacterial in near the beginning of 30 s was the opening of most charming period of chemotherapeutic agents [1-4].

Sulfonamide groups are not only antibacterial but are considered as a phramacophore which is present in a number of biologically active molecules, particularly in antimicrobial agents [5-9], additional to this many sulfonamides derivatives have been reported as carbonic anhydrase inhibitors [10-14], anticancer [15] and anti-inflammatory agents [16].

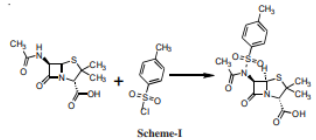
Some organism become resistant to all approved antibiotics and for their treatment there is need of potentially toxic drugs. There is overpowering need to build up highly effective and valuable antibacterial agents in order to treat infections which are caused by bacterial pathogens (resistant to existing antibiotics). Sulfonamides have broad spectrum of antibacterial activity because they behave as competitive inhibitors of enzymes dihydropteroate synthase (DHPS) and also having adverse effects especially in HIV patients [17]. As sulfonamides are inexpensive and highly active group so synthesis of novel sulfonamides with high activity is of great interest for pharmaceutical industry. The present study deals with synthesis of some new sulfonamides. The structure of synthesized compounds was recognized and confirmed by elemental analysis and from data obtained by spectral analysis *i.e.* IR, H NMR, ESI-MS and λ_{max}. Biological activity was studied using Gram-positive and Gram-negative strains of bacteria.

EXPERIMENTAL

p-Toluenesulphonyl chloride, penicillin, amoxicillin, cefixime, sodium carbonate and all solvents used were purchased from sigma Aldrich. Purification of synthesized compounds were done by precoated silica gel plates (Germany, Merck). Melting points were taken by using Gallen hamp apparatus. IR spectra for new compounds were obtained in range between 4000-600 cm^{-1} on Cary 630 Agilent FTIR spectrophotometer. PG-T90$^+$ UV-visible spectrophotometer for λ_{max} and flash HT plus elemental analyzer for analysing % of H, C, N and S, were used respectively. For mass determination of new molecules mass spectrometer having following specification was used Model: 6200 Series accurate-Mass, resolution: > 20,000 resolving power, ionization method: electrospry (ESI) Scanning speed: up to 40 spectra per second Mass range: 20 to 20,000 *m/z* Dynamic range: 10^5. ^{1}H NMR spectra in DMSO of synthesized compounds were recorded on Bruker AC-iii 300 MHz instrument at 300 K, Chemical shifts were reported in δ (ppm) with respect to TMS as an internal standard; coupling constants were expressed in Hertz.

Synthesis of N-((2S,5R,6R)-2-formyl-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptanes-6-yl)-N-tosylacetamide (1): Penicillin (0.835 g, 0.1 mol) was taken in 25 mL water. It was stirred and pH was checked at regular intervals. After maintaining pH at 9 (0.264 g, 0.1 mol) *p*-toluene sulfonyl chloride was added. Stirring of this reaction mixture was continued and reaction completion was monitored by TLC. In order to precipitate the product 1 N HCl was added by maintaining the pH of reaction mixture at 2-3. Product was separated by filtration and recrystillized using ethanol (**Scheme-I**). Purification of product was confirmed by TLC using mobile phase of dichloromethane:ethanol (50:50).

IR (film, ν_{max}, cm^{-1}): 1150.35 (N-S=*O* str.), 1055.12 (C-N str), 1641.45 (-N-*C*=*O*), 815.32 (C-S str), 930.16 (S-N str), 3388.12 (-OH). δ_H (300 MHz; DMSO): 9.28 (1H, s, -OH), 7.22-7.47 (4H, m, Ar*H*), 5.14-5.27 (1H, d, *J* = 6.9, -COC*H*N-), 4.10 (1H, s, -*CH*COOH), 4.00-4.03 (1H, d, *J* = 6.9, -C*H*S (CH$_3$), 2.49 (3H, s, -TsC*H*$_3$), 2.32 (3H, s, -COC*H*$_3$), 1.88 (6H, s, -C(C*H*$_3$)$_2$); *m/z* (ESI) 412; HRMS (ESI) calcd. for $C_{17}H_{20}N_2O_6S_2$; $C_{17}H_{20}N_2O_6S_2Na^+$ 435.13. Mass analysis for mass 435.1381000 and found to be 435.1392490. Anal. calcd. for $C_{17}H_{20}N_2O_6S_2$ (m.w. 412): C, 49.50; H, 4.89; N, 6.79; S,15.55 %. Found: C, 49.48; H, 4.87; N, 6.77; S, 15.53 %.



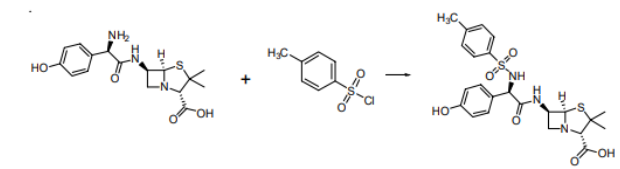
Scheme-I

Synthesis of (2S,5R,6R)-6-((R)-2-(4-hydroxyphenyl)-2-(4-methylphenylsulfonamido)acetamido)-3,3-dimethyl-4-thia-1-azabicyclo[3,2,0]heptanes-2-carboxylic acid (2): (0.9125 g, 0.1 mol) amoxicillin was dissolved in 25 mL water in a round bottom flask and stirred for some time. pH was checked and maintained at 8-9. Then (0.264 g, 0.1 mol) *p*-toluene sulfonyl chloride was added to the above reaction mixture and pH was strictly maintained at 8-9. Reaction mixture was stirred for 2-3 h at room temperature and reaction completion was monitored by TLC. After reaction completion 1 N HCl was added and product was precipitated out at pH 2-3. After filtration purification was done by recrystallization from ethanol (**Scheme-II**). Product purification was confirmed by TLC using mobile phase of acetic acid:butanol:water (10:70:20).

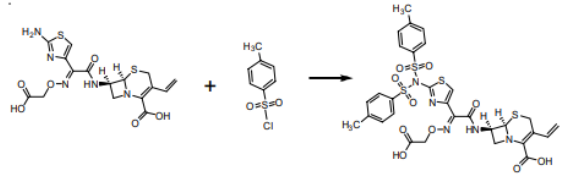
IR (film, ν_{max}, cm^{-1}): 1148.67 (N-S=*O* str), 1050.4 (C-N str), 1641.88 (-N-*C*=*O*), 814.49 (C-S str), 932.6 (S-N str,), 3239.36 (OH). δ_H (300 MHz; DMSO): 9.48 (1H, s,-COO*H*), 8.45-8.54 (1H, d, *J* = 6.5 -N*H*CO-), 8.14-8.27 (1H, d, *J* = 6.9-N*H*SO$_2$-), 7.03-7.73 (8H, m, Ar*H*), 6.75 (1H, s, Ar-O*H*), 6.48-6.51 (1H, d, *J* = 6.7,-*CH*NHSO$_2$), 6.03-6.31 (1H, q, *J* = 6.6, -*CH*NHCO), 5.73-5.89 (1H, d, *J* = 6.6-C*H*S (CH$_3$)$_2$), 5.53 (1H, s,-*CH*COOH), 4.89-5.27 (1H, dd, *J* = 6.5, 1.2, -*CH*HN), 4.20-4.60 (1H, dd, *J* = 6.4, 1.2, -CH*H*N), 3.32 (3H, s, ArC*H*$_3$), 2.31 (6H, s, -C (C*H*$_3$)$_2$); *m/z* (ESI) 505.13; HRMS (ESI) calcd for $C_{23}H_{27}N_3O_8S_2$; $C_{23}H_{27}N_3O_8S_2Na^+$ 528.23 Mass analysis for mass 528.2301450 and found to be 528.2390850. Anal. calcd. for $C_{23}H_{27}N_3O_8S_2$ (m.w. 505.61): C, 54.64; H, 5.38; N, 8.31; S, 12.68 %. Found: C, 54.62; H, 5.36; N, 8.29; S, 12.66 %.

Synthesis of (6R,7R)-7-((E)-2-((carboxymethoxy)imino)-2-(2-(4-methyl-N-tosylphenylsulfonamido)thiazol-4-yl)-acetamido)-3-vinyl-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid (3): (1.33 g, 0.1 mol) cefixime was dissolved in 25 mL water, when pH of solution became 9 then (0.264 g, 0.1 mol) *p*-toluene sulfonyl chloride was added. This reaction mixture was stirred at room temperature; under controlled pH. Monitoring of preceding reaction was done by use of TLC. At the end of reaction 1 N HCl was added, product was precipitated out at pH 2-3, which was separated out by filtration (**Scheme-III**). Purification of product was performed by recrystillization using methanol. TLC of purified product was done using mobile phase dichloromethane:ethanol (60:40).

IR (film, ν_{max}, cm^{-1}): 1159.48 (N-S=*O* str), 1086 (C-N), 1652.80 (-N-*C*=*O*), 819.62 (C-S), 958.92 (S-N). δ_H (300 MHz; $CDCl_3$): 11.07 (1H, s,-COO*H*), 10.56 (1H, s,-COO*H*), 8.48-8.52 (1H, d, *J* = 6.3 -N*H*CO-), 7.94-8.25 (4H, m, Ar*H*), 7.79 (1H, s, -C=C*H*S-), 7.54-7.64 (4H, m, Ar*H*), 6.64-6.78 (1H, dd, *J* = 6.3, 1.3, -*CH*=CH$_2$), 5.83-5.88 (1H, d, *J* = 6.5,-*CH*N (S)), 5.42-5.50 (1H, dd, *J* = 6.4, 1.4, -CH=C*H*H), 5.21-5.32 (1H, dd, *J* = 7.1, 1.3, -CH=CH*H*), 5.08 (1H, s, -OC*H*$_2$COOH), 4.86-4.97 (1H, q, *J* = 6.5, -*CH*NHCO), 3.48-3.66 (1H, dd, *J* = 6.2, 1.2, -*CH*HN), 3.23-3.35 (1H, dd, *J* = 6.3, 1.2, -CH*H*N), 3.95-3.03 (2H, dd, *J* = 4.3, 1.4,-C*H*HS), 2.34 (6H, s, -Ar (C*H*$_3$)$_2$); *m/z* (ESI) 747.84; HRMS (ESI) calcd for $C_{35}H_{29}N_5O_{10}S_4$; $C_{35}H_{29}N_5O_{10}S_4Na^+$ 770.92 Mass analysis for mass 747.9210341 and found to be 747.9223402. Anal. calcd. for $C_{35}H_{29}N_5O_{10}S_4$ (m.w. 747.84): C, 48.18; H, 3.91; N, 9.36; S, 17.15 %. Found: C, 48.16; H, 3.89; N, 9.34; S, 17.13 %.



Scheme-II



Scheme-III

TABLE-1
PHYSICAL PROPERTIES OF SYNTHESIZED COMPOUNDS

Compd.	m.f.	Colour of compounds	R_f value	λ_{max} *	m.p. (°C)	Yield (%)
1	$C_{23}H_{26}N_2O_6S_2$	Green	1.20	270	240	56
2	$C_{23}H_{27}N_3O_8S_2$	Light green	0.44	255	210	55
3	$C_{35}H_{29}N_5O_{10}S_4$	Light brown	0.33	289	180	77

*Solvent used for λ_{max} was ethanol for all compounds.

Antibacterial assay: Luria-Bertani broth was used as a growth medium due to it efficient results in bacterial growth [17]. LB broth was prepared by taking 4 g of tryptone, 2 g of yeast extract and 4 g of sodium chloride in 400 mL of distilled water, using NaOH (1 N) pH was maintained at 7. This prepared medium was autoclaved at 125 °C for 0.5 h. Sample solutions were prepared in ethanol and ethanol was also used as control. Using micropipette different volumes of samples were taken in appendroff tubes. All this process was done in Laminar flow of BSL-2 in order to keep contamination away.

Each sample was screened against two bacterial strains, in 5-50 µg concentration range. For each bacterial strain 3 test tubes were labelled. 2 mL of LB broth and 20 µL of bacterial strains [Gram-positive (*Staphylococcus aureus*) and Gram-negative (*Escherichia coli*)] were added in these tubes. After that stocks of 5 µL, 10 µL, 20 µL containing 5 µg, 12.5 µg and 50 µg were added. These tubes were incubated at 37 °C for complete 24 h. After this optical density of each medium and control medium was taken at 600 nm.

RESULTS AND DISCUSSION

Synthesized sulphonamides are soluble in common organic solvents. Physical properties of synthesized sulphonamides are given in Table-1.

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In compound **2**, there is a diasterocentre *i.e.* -CH^{a}H^b present in the four member ring. Both protons in -CH_2 are different from each other, coupled with each other to give a doublet and that doublet is further coupled with neighbouring ^{1}H to give a doublet of doublet. Two doublets of doublet were found at 4.89-5.27 and 4.20-4.60 ppm, respectively.

In compound **3**, chemical shift values were calculated for a diasterocentre at 3.48-3.66 and 3.23-3.35 ppm respectively. In this molecule, there is vinyl group (-CH=CH_2-) in which all three protons are chemically non-identical and every one gave a doublet of a doublet. Their activities against both bacterial strains are shown in Table-2.

TABLE-2
IC_{50} DETERMINATION OF DIFFERENT SYNTHETIC PRODUCTS AGAINST DIFFERENT STRAINS OF BACTERIA

Compound No.	*S. aureus*	*E. coli*
1	5 µg	5 µg
2	–	5 µg
3	12.5 µg	50 µg

Note: The amount of compound at which 50 % bacterial growth is inhibited with reference to control is called IC_{50} value.

Minimum inhibition concentration values for all synthesized sulphonamides shows a discrepancy between 5 to 50 µg. It is clear that best MIC values for both strains were obtained by new sulphonamide molecule compound **1** *i.e.* 5 µg, however compound **2** showed good result for only one strain that is *S. aureus* having IC_{50} value at concentration of 5 µg and com-

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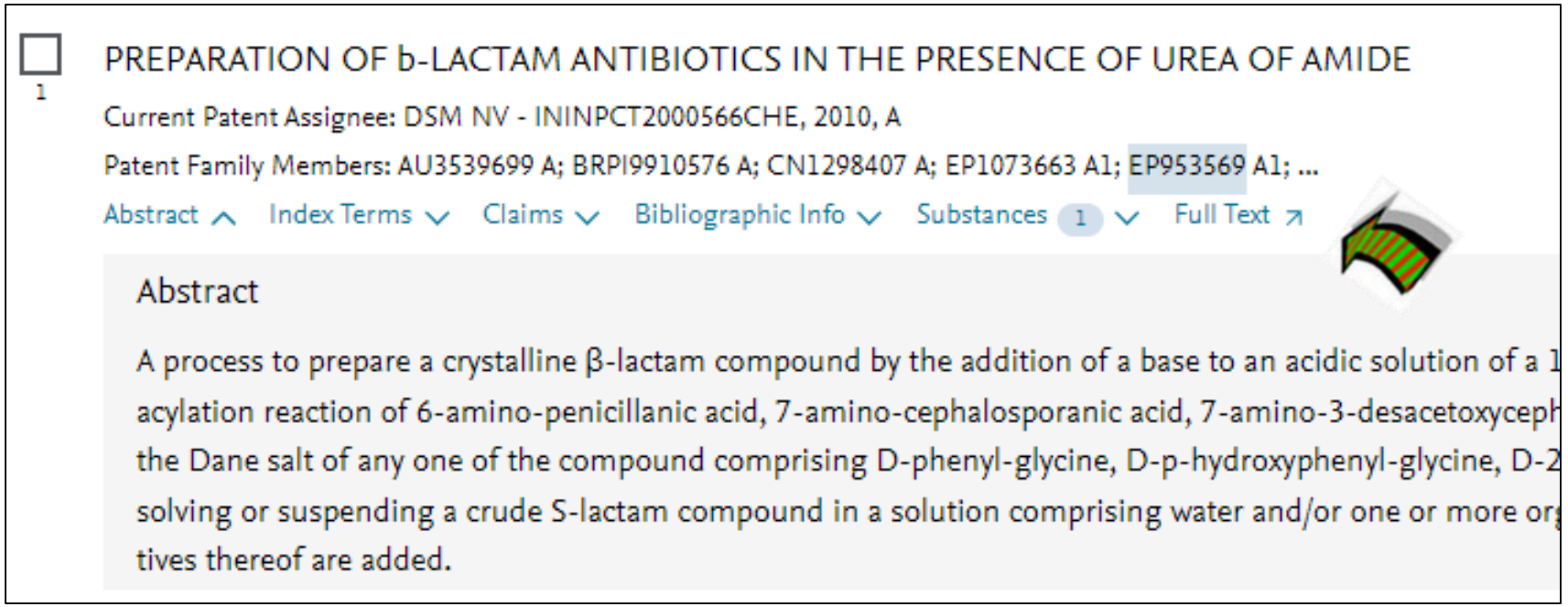
   In one or two sentences what is novel or unique about this patent and these claim(s)?

   _____

Leenderts, E J A. Preparation of beta-lactam antibiotics in the presence of urea or amide. EP 0953569A1, Nov 3, 1999.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PREPARATION OF b-LACTAM ANTIBIOTICS IN THE PRESENCE OF UREA OF AMIDE
Current Patent Assignee: DSM NV - ININPCT2000566CHE, 2010, A
Patent Family Members: AU3539699 A; BRPI9910576 A; CN1298407 A; EP1073663 A1; EP953569 A1; ...
Abstract
Index Terms
Claims
Bibliographic Info
Substances 1
Full Text
Abstract
A process to prepare a crystalline β-lactam compound by the addition of a base to an acidic solution of a 1
acylation reaction of 6-amino-penicillanic acid, 7-amino-cephalosporanic acid, 7-amino-3-desacetoxycepl
the Dane salt of any one of the compound comprising D-phenyl-glycine, D-p-hydroxyphenyl-glycine, D-2
solving or suspending a crude S-lactam compound in a solution comprising water and/or one or more or
tives thereof are added.

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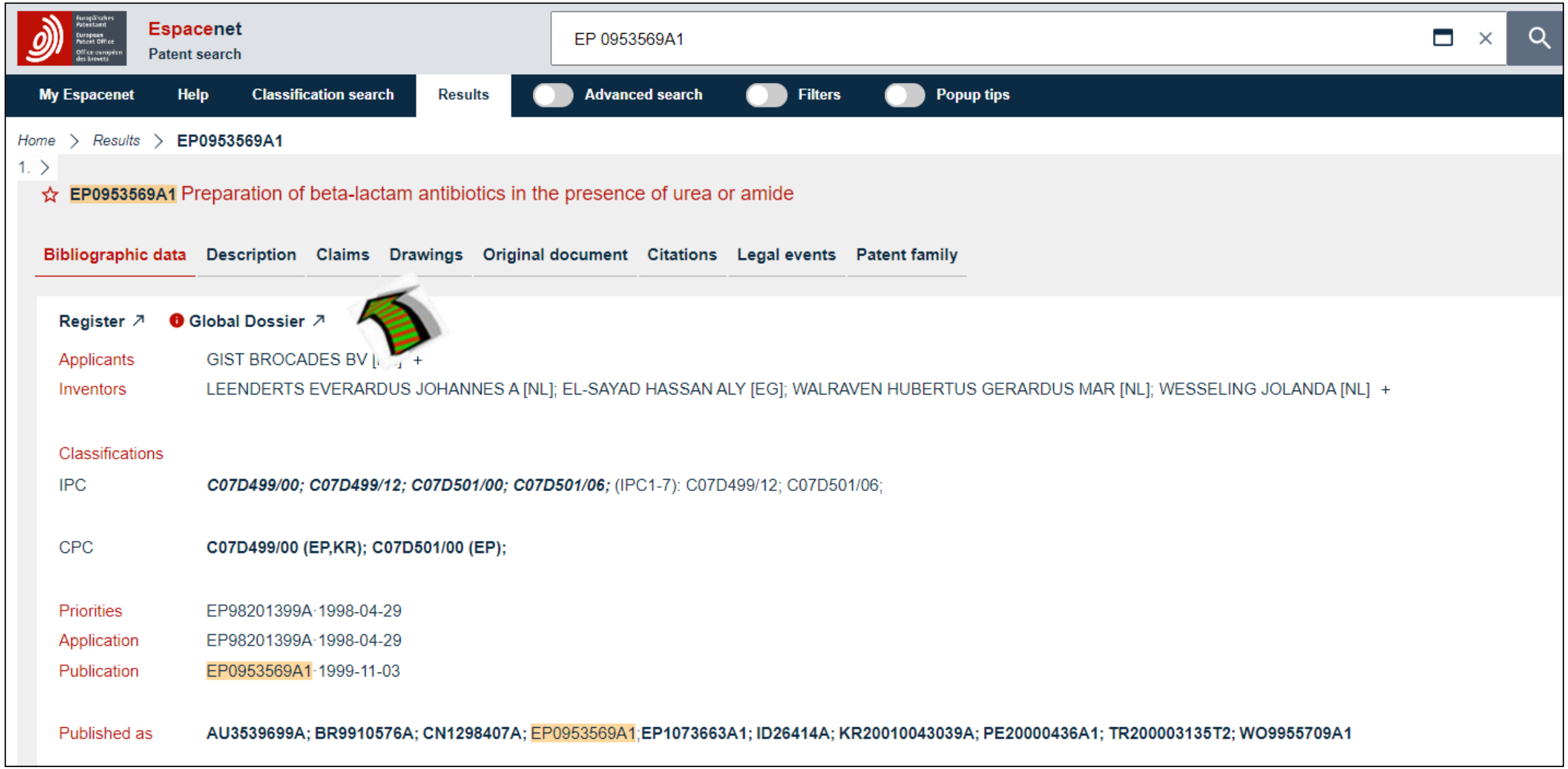

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9. You've been hired by an international pharmaceutical company as a researcher / chemist / scientist and challenged to respond to the CDC's 2019 AR Threats Report. Read the entire document! Using your favorite scholarly database, find a recent scholarly peer-reviewed experimental biochemistry, biological, pharmacology, biomedical, or chemistry journal article **using one of the 18 antibiotic-resistant bacteria or fungi** that speaks to this threat. This article has to include experimental methodology and data to answer question 10. Cite this paper using ACS Citation (with title):

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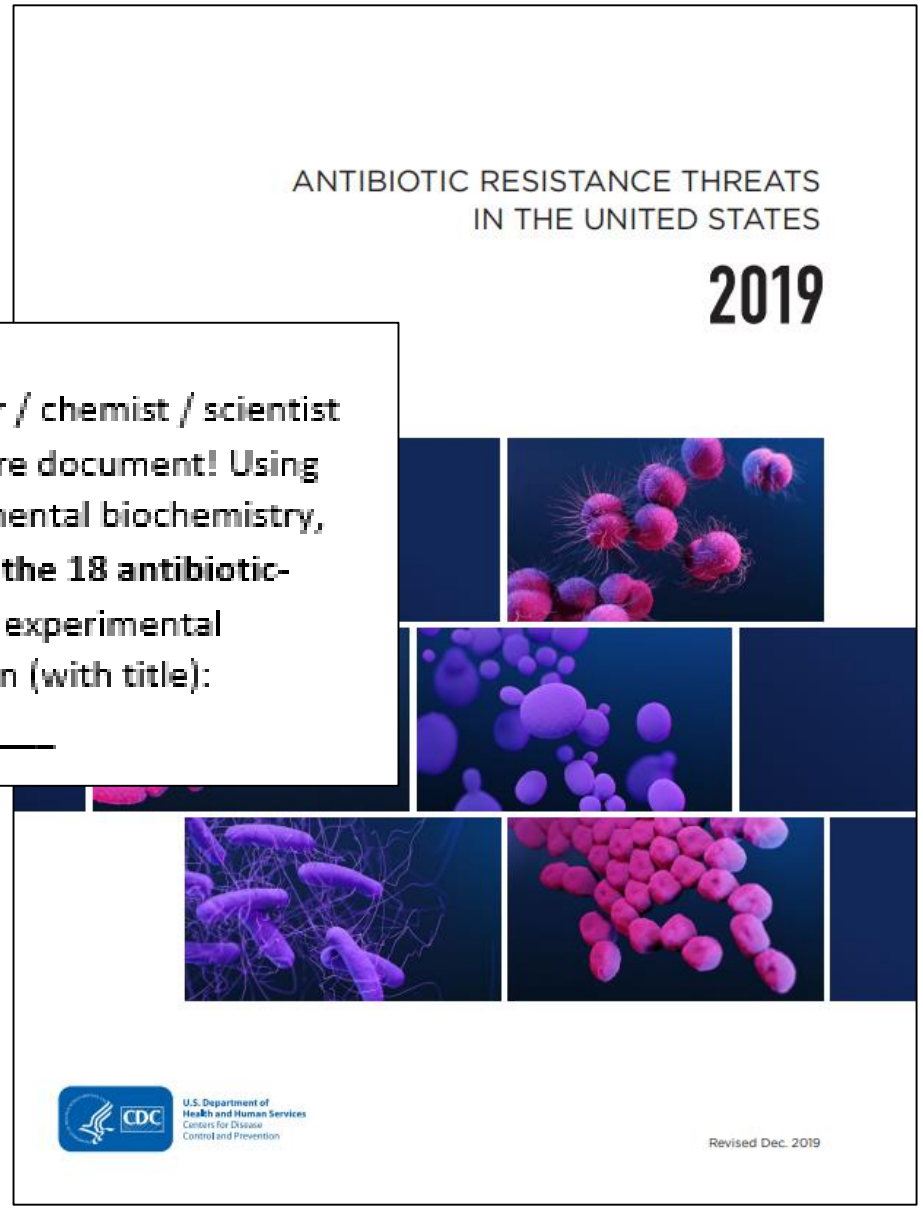

Urgent Threats

- Carbapenem-resistant *Acinetobacter*
- *Candida auris (C. auris)*
- *Clostridioides difficile (C. difficile)*
- Carbapenem-resistant Enterobacteriaceae (CRE)
- Drug-resistant *Neisseria gonorrhoeae (N. gonorrhoeae)*

Serious Threats

- Drug-resistant *Campylobacter*
- Drug-resistant *Candida*
- Extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae
- Vancomycin-resistant *Enterococci* (VRE)
- Multidrug-resistant *Pseudomonas aeruginosa (P. aeruginosa)*
- Drug-resistant nontyphoidal *Salmonella*
- Drug-resistant *Salmonella* serotype Typhi
- Drug-resistant *Shigella*
- Methicillin-resistant *Staphylococcus aureus* (MRSA)
- Drug-resistant *Streptococcus pneumoniae (S. pneumoniae)*
- Drug-resistant Tuberculosis (TB)

Concerning Threats

- Erythromycin-resistant group A *Streptococcus*
- Clindamycin-resistant group B *Streptococcus*

Watch List

- Azole-resistant *Aspergillus fumigatus (A. fumigatus)*
- Drug-resistant *Mycoplasma genitalium (M. genitalium)*
- Drug-resistant *Bordetella pertussis (B. pertussis)*

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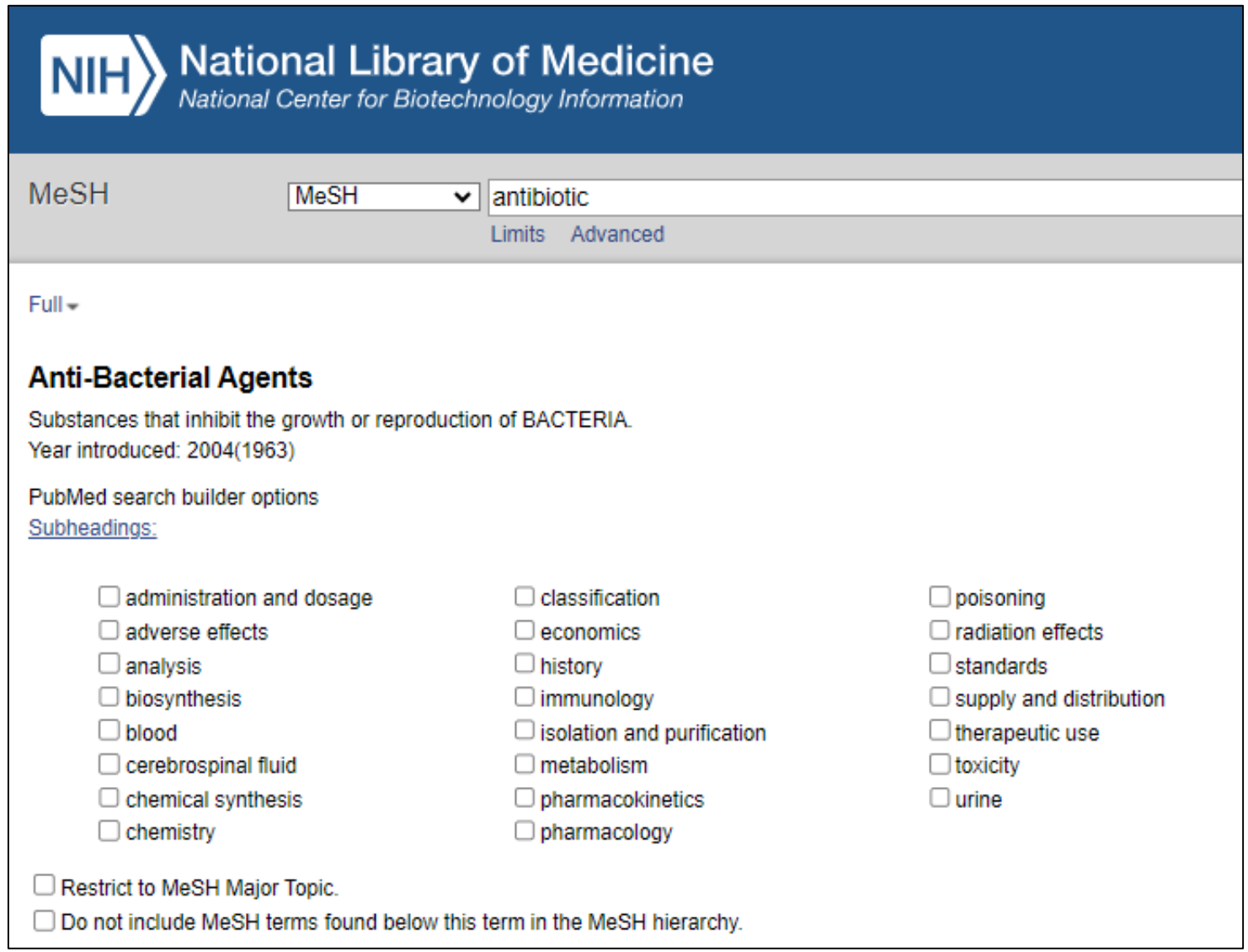

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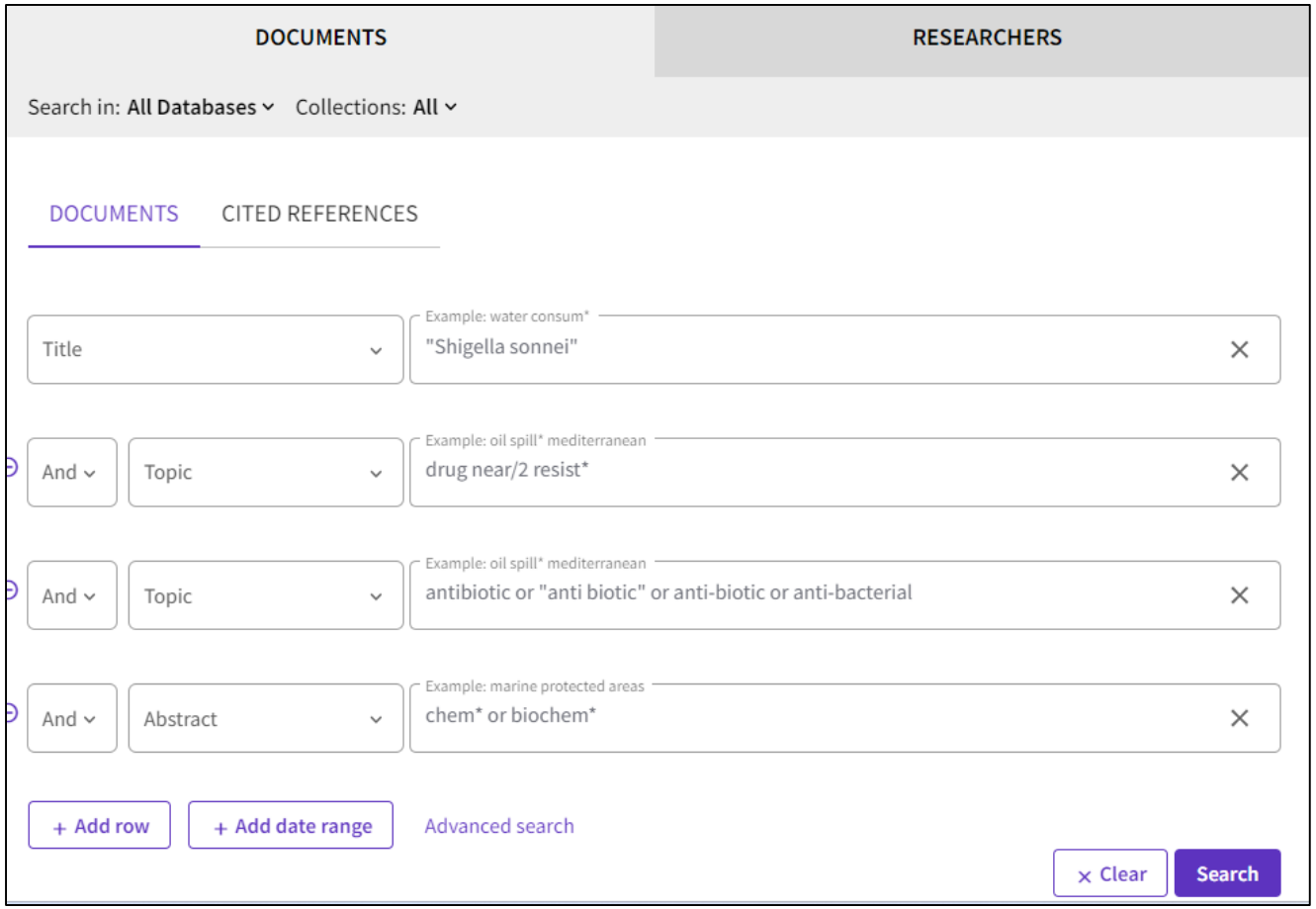

Exploratory N-Protecting Group Manipulation for the Total Synthesis of Zwitterionic *Shigella sonnei* Oligosaccharides

By Dhara, D (Dhara, Debashis) [1] ; Mulard, LA (Mulard, Laurence A.) [1]

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Keywords **Author Keywords:** AAT; altrose; glycosylation; protecting groups; zwitterionic polysaccharides

Keywords Plus: CONJUGATE VACCINE CANDIDATE; O-SPECIFIC POLYSACCHARIDE; REPEATING UNIT; FLEXNERI SEROTYPE-2A; GLYCOSYL ACCEPTORS; GANGLIOSIDE SERIES; CHEMICAL-SYNTHESIS; NMR-SPECTROSCOPY; ANTIGEN; DERIVATIVES

MeSH terms

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- Glycosylation
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Abstract

Shigella sonnei surface polysaccharides are well-established protective antigens against this major cause of diarrhoeal disease. They also qualify as unique zwitterionic polysaccharides (ZPSs) featuring a disaccharide repeating unit made of two 1,2-*trans* linked rare aminodeoxy sugars, a 2-acetamido-2-deoxy-L-altruronic acid (L-Alt*p*NAcA) and a 2-acetamido-4-amino-2,4,6-trideoxy-D-galactopyranose (AAT). Herein, the stereoselective synthesis of *S. sonnei* oligosaccharides comprising two, three and four

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Total Synthesis

Exploratory N-Protecting Group Manipulation for the Total Synthesis of Zwitterionic *Shigella sonnei* Oligosaccharides

Debashis Dhara and Laurence A. Mulard*[a]

Abstract: *Shigella sonnei* surface polysaccharides are well-established protective antigens against this major cause of diarrhoeal disease. They also qualify as unique zwitterionic polysaccharides (ZPSs) featuring a disaccharide repeating unit made of two 1,2-*trans* linked rare aminodeoxy sugars, a 2-acetamido-2-deoxy-L-altruronic acid (L-Alt*p*NAcA) and a 2-acetamido-4-amino-2,4,6-trideoxy-D-galactopyranose (AAT). Herein, the stereoselective synthesis of *S. sonnei* oligosaccharides comprising two, three and four repeating units is reported for the first time. Several sets of up to seven protecting groups were explored, shedding light on the singular conformational behavior of protected altrosamine and altruronic residues. A disaccharide building block equipped with three distinct *N*-protecting groups and featuring the uronate moiety already in place was designed to accomplish the iterative high yielding glycosylation at the axial 4-OH of the altruronate component and achieve the challenging full deprotection step. Key to the successful route was the use of a diacetyl strategy whereby the *N*-acetamido group of the L-Alt*p*NAcA is masked in the form of an imide.

Introduction

Diarrheal diseases are a major public health burden worldwide and the second leading-cause of death in children under 5 years of age. Two recent keynote studies—the GEMS[1] and the MAL-ED[2]—have identified *Shigella* as one of the top agents causing moderate-to-severe diarrhea in this population. Still, the global burden of shigellosis is thought to be underestimated and the emergence of multidrug-resistant strains goes against antibiotic treatment as being the sole answer to *Shigella* burden.[3] Fighting shigellosis by means of vaccines was recommended decades ago by WHO and vaccination is still viewed as a valuable preventive intervention. However, no broadly licensed *Shigella* vaccine is available despite a diversity of vaccine candidates tested in clinical trials.[4] *Shigella sonnei*, as a single serotype, causes an estimated 25% of all shigellosis episodes. It is the second most common *Shigella* species in low and middle income countries and the predominant species in high income and transitional countries.[5] High incidence in traveler's diarrhea and increasing antibiotic resistance also contribute to concern for this Gram negative enteroinvasive bacterium.[6] Evidence point to *S. sonnei* surface lipopolysaccharide as being the major protective antigen against reinfection,[7] and among the many strategies under investigation toward a *S. sonnei* vaccine, polysaccharide conjugates have emerged as a promising route.[8] Otherwise, exploring the feasibility of using synthetic carbohydrate haptens as surrogates of the *S. sonnei* natural polysaccharide antigens is envisioned as a promising alternative. It is noteworthy that this strategy was originally investigated in our group to tackle a *Shigella flexneri* 2a infection.[9] A vaccine candidate featuring a 15-mer oligosaccharide hapten—a trimer analogue of the biological repeating unit of the *S. flexneri* 2a O-antigen (O-Ag)—linked to a protein carrier via single point attachment was proposed,[10] and more recently demonstrated to be safe and strongly immunogenic in adult volunteers.[11] Now paying attention to the second most prevalent *Shigella* serotype, we report herein our exploratory work and successful achievements on the chemical synthesis of oligomers of the repeating unit from the *S. sonnei* O-Ag, a unique zwitterionic polysaccharide (ZPS). *S. sonnei* is to our knowledge, the only *Shigella* surrounded by a capsular polysaccharide (CPS). As recently disclosed, the two *S. sonnei* surface polysaccharides display the same zwitterionic repeating unit.[12] Therefore, our effort aims in the long run at a *S. sonnei* vaccine candidate capable at inducing both an anti-LPS and an anti-CPS antibody-mediated protective response.

As for other ZPSs, the zwitterionic character of the surface polysaccharides from *S. sonnei* stems from adjacent monosaccharide units harboring alternating charges within the repeating unit. But to our knowledge, the *S. sonnei* ZPSs are the sole as of to date featuring a disaccharide repeating unit. The latter

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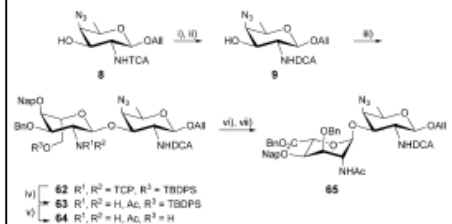
and 73%, respectively. The drastic difference in the solubility of the DCA intermediates with respect to their TCA analogues noticeably impaired the easy manipulation of the former and building block **65** was not investigated further.



Scheme 8. Synthesis of the AB building block **65** by means of a [A + B] glycosylation using the orthogonally protected A donor **33** and acceptor **9**. (i) LiOH.H_2O, Acet/H_2O (2:1, v/v), 50 °C, (ii) DCA-Cl, Et_3N, ACN, 68% over two steps, (iii) Crude **33**, TMSOTf, ACN, −15 °C, 67%, (iv) *a*. Ethylenediamine, MeOH/THF (1:1, v/v), 50 °C, *b*. Ac_2O, MeOH, 87%, (v) TBAF, THF, 80%, (vi) TEMPO, BAIB, DCM/H_2O, (vii) BnBr, K_2CO_3, DMF, 61% over 2 steps. ACN: acetonitrile.

This outcome led us to focus on the strategy featuring the more promising 2_A-NAc_2/2_B-NTCA AB building b
met when attempting the 2_A-NAc_2 to 2_A-NAc co
mild basic conditions (Scheme S6) urged us to
leading "single step full deprotection" concept
vestigate a two-step deprotection strategy whe
lation at position 2_A would only occur post ber
age (Scheme 9). As a follow up of our pre

MS/HRMS monitoring to ensure full hydrodechlorination, and subsequent *N*-deacetylation of the crude intermediate gave the desired AB propyl glycoside **1** in a good 57% yield from disaccharide **47**. The same conditions applied to tetrasaccharide **52** and hexasaccharide **54** furnished the more complex $[AB]_2$ and $[AB]_3$ zwitterionic targets in 6 to 12 mg amount, in a moderate 39% and 31% yield post RP-HPLC purification, respectively. Extrapolation to the fully protected **56** also exemplified the feasible two-step conversion to the more demanding $[AB]_4$ zwitterionic octasaccharide. These achievements open for the first time the way to large oligosaccharides representative of the unique *S. sonnei* and *P. shigelloides* O17 ZPS antigens.

Conclusions

In this study, we have embarked on the block wise synthesis of oligosaccharides encompassing multiple repeating units of the ZPSs from *S. sonnei*. To reach our objective, we have reinvestigated the protecting group pattern of a suitable ready-for-oligomerization disaccharide building block, corresponding to the AB repeating unit. Aiming at avoiding the extensive hydrodechlorination associated to the necessary conversion of multiple trichloroacetamides into acetamides featured in the originally designed 2_A-NTCA,2_B-NTCA AB brick,[24] alternative routes were explored, whilst a final hydrogenation/hydrogenolysis

Propyl (2-acetamido-2-deoxy-α-L-altropyranosyluronic acid)-(1→3)-(2-acetamido-4-amino-2,4,6-trideoxy-β-D-galactopyranosyl)-(1→4)-(2-acetamido-2-deoxy-α-L-altropyranosyluronic acid)-(1→3)-(2-acetamido-4-amino-2,4,6-trideoxy-β-D-galactopyranosyl)-(1→4)-(2-acetamido-2-deoxy-α-L-altropyranosyluronic acid)-(1→3)-2-acetamido-4-amino-2,4,6-trideoxy-β-D-galactopyranoside (3): Hexasaccharide **54** (70 mg, 31 µmol, 1.0 equiv) was dissolved in *t*BuOH/DCM/H_2O (19 mL, 20:5:2, v/v/v). 20% $Pd(OH)_2$/C (120 mg) was added and the suspension was degassed repeatedly. After stirring under a hydrogen atmosphere for 48 h, monitoring by LCMS analysis showed the presence of the targeted intermediate (LCMS: $[M+H]^+$ *m/z* 1396.4). The suspension was passed through a 0.2 µm filter and washed extensively with methanol. The filtrate was concentrated and the crude material was dried under vacuum for 2 h. The obtained white powder was dissolved in methanol (3.0 mL) and hydroxylamine (6.1 mg, 85 µmol, 3.0 equiv) was added. After stirring for 3 h, LCMS analysis showed the complete disappearance of the triacetate intermediate and the presence of the desired product (LCMS: $[M+H]^{2+}$ *m/z* 635.2). Water (6.0 mL) was added and the reaction mixture was lyophilized. Purification of the crude material by semi-preparative RP-HPLC gave hexasaccharide **3** as a white solid (12 mg, 9.4 µmol, 31%). The propyl glycoside **3** had RP-HPLC (215 nm) Rt = 11.3 min (conditions A), Rt = 13.3 min (conditions B). ^{1}H NMR (D_2O) δ 4.88 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1_{A2}), 4.78 (d_{po}, 2H, $J_{1,2}$ = 8.4 Hz, H-1_A, H-1_{A1}), 4.75 (d_{po}, 1H, $J_{1,2}$ = 8.4 Hz, H-1_{B1}, H-1_{B2}), 4.70 (brs_{po}, 2H, H-5_A, H-5_{A1}), 4.61 (brs, 1H, H-5_{A2}), 4.46–4.44 (m_{po}, 2H, H-1_B, H-4_A), 4.36 (brs, 1H, H-4_{A1}), 4.16–4.09 (m, 3H, H-3_B, H-3_{B1}, H-3_{B2}), 4.06–3.90 (m, 7H, H-5_B, H-5_{B1}, H-5_{B2}, H-2_A, H-2_{A1}, H-4_A, H-4_B), 3.86–3.72 (m, 10H, H-3_A, H-3_{A1}, H-3_{A2}, H-4_{B1}, H-4_{B2}, H-2_A, H-2_B, H-2_{B1}, H-2_{B2}, OCH_{2Pr}), 3.51–3.49 (m_{po}, 1H, OCH_{2Pr}), 1.99, 1.98, 1.96, 1.95 (4 s, 18H, CH_{3Ac}), 1.54–1.45 (m, 2H, CH_{2Pr}), 1.30–1.29 (d_{po}, 9H, H-6_B), 0.82 (t, 3H, J = 7.2 Hz, CH_{3Pr}).^{13}C NMR (D_2O) δ 174.6, 174.5, 174.4, 174.0 (6C, CO_{NAc}), 172.6, 172.2 (C-6_A, C-6_{A1}, C-6_{A2}), 102.9, 102.8 (C-1_A, C-1_A, C-1_A, $^1J_{C,H}$ = 174.2 Hz, $^1J_{C,H}$ = 170.2 Hz), 101.6 (C-1_B, $^1J_{C,H}$ = 162.0 Hz), 101.2, 101.1 (C-1_{B1}, C-1_{B2}, $^1J_{C,H}$ = 166.2 Hz), 76.6 (C-4_A, C-4_{A1}), 76.3, 76.1 (C-5_A, C-5_{A1}, C-5_{A2}), 75.7 (C-3_B, C-3_{B1}, C-3_{B2}), 72.7 crude material by semi-preparative RP-HPLC gave octasaccharide **4** as a white solid (1.7 mg, 1.01 µmol, 16%). The propyl glycoside **4** had RP-HPLC (215 nm) Rt = 11.3 min (conditions A'). ^{1}H NMR (D_2O, 800 MHz) δ 4.81–4.79 ($2d_{po}$, 3H, H-1_A), 4.67–4.65 (m_{po}, 4H, H-1_A, 3H-1_B), 4.54 (brd_{po}, 2H, H-4_A), 4.42–4.37 (brs, 4H, 3H-5_A, H-1_B), 4.31–4.30 (m_{po}, 3H, H-5_A, 2H-4_A), 4.11–4.05 (m, 4H, H-3_B), 4.01–3.99 (q, 4H, H-5_B), 3.92–3.87 (m, 3H, H-2_B, 2H-4_B), 3.82–3.68 (m, 9H, 4H-2_A, 3H-2_B, 2H-4_B), 3.67–3.65 (m_{po}, 3H, 2H-3_A, OCH_{2Pr}), 3.59–3.55 (m_{po}, 3H, 2H-3_A, OCH_{2Pr}), 1.96–1.89 (m_{po}, 24H, CH_{3Ac}), 1.47–1.44 (m, 2H, CH_{2Pr}), 1.26 (m_{po}, 12H, H-6_B), 0.78 (t, 3H, J = 7.2 Hz, CH_{3Pr}). ^{13}C NMR (D_2O, 800 MHz) δ 174.8, 174.6, 174.4, 173.9 (8C, CO_{NAc}), 163.1, 162.9 (4C, C-6_A), 103.0 (2C, C-1_A), 101.6 (C-1_A, C-1_B), 101.1 (2C, C-1_B), 100.9 (C-1_B, C-1_A), 77.9, 77.4, 77.3 (3C, C-4_A), 76.0, 75.8, 75.7, 75.5 (4C, C-3_B), 72.6 (OCH_{2Pr}), 72.0 (C-4_{A3}), 69.1, 68.1, 67.7 (4C, C-3_A), 67.4, 67.2 (4C, C-5_B), 54.9, 54.7 (4C, C-4_B), 51.4 (4C, C-2_A), 50.9, 50.8 (4C, C-2_B), 22.3, 22.1 (8C, CH_{3Ac}), 21.2 (CH_{2Pr}), 15.5 (4C, C-6_B), 9.4 (CH_{3Pr}). HRMS (ESI^+): *m/z* $[M+2H]^{2+}$ calcd for $C_{61}H_{110}N_{12}O_{37}$ 837.3547; found 837.3542.

Supporting Information: The Supporting Information contains the following: Schemes S1–S6 and Tables S1–S3. General procedures. Experimental procedures and analytical data for compounds **1**, **2**, **9–11**, **14–19**, **21–29**, **38–41**, **57–65**, **S1–S4** and **S7–S10**. ^{1}H and ^{13}C NMR spectra of novel compounds.

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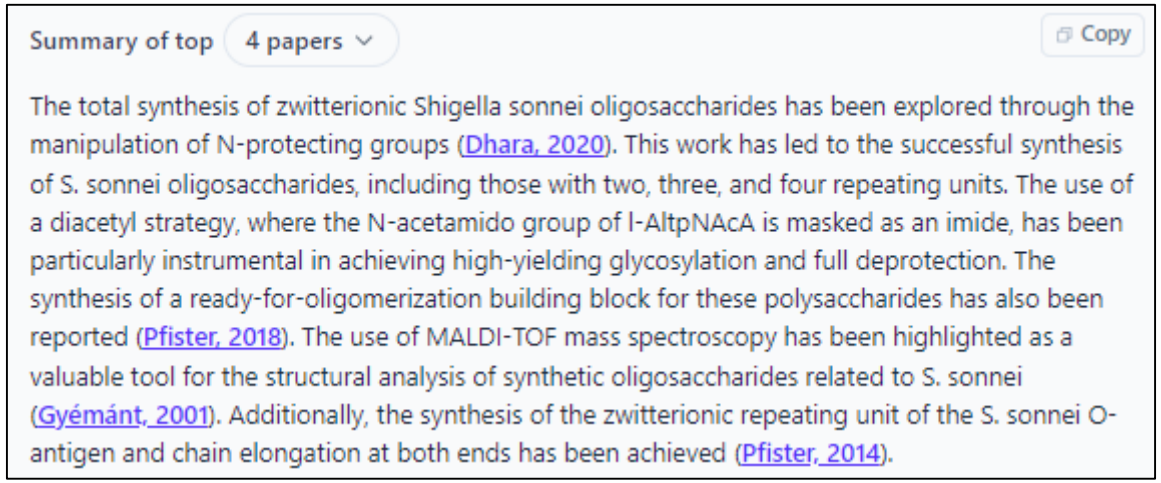
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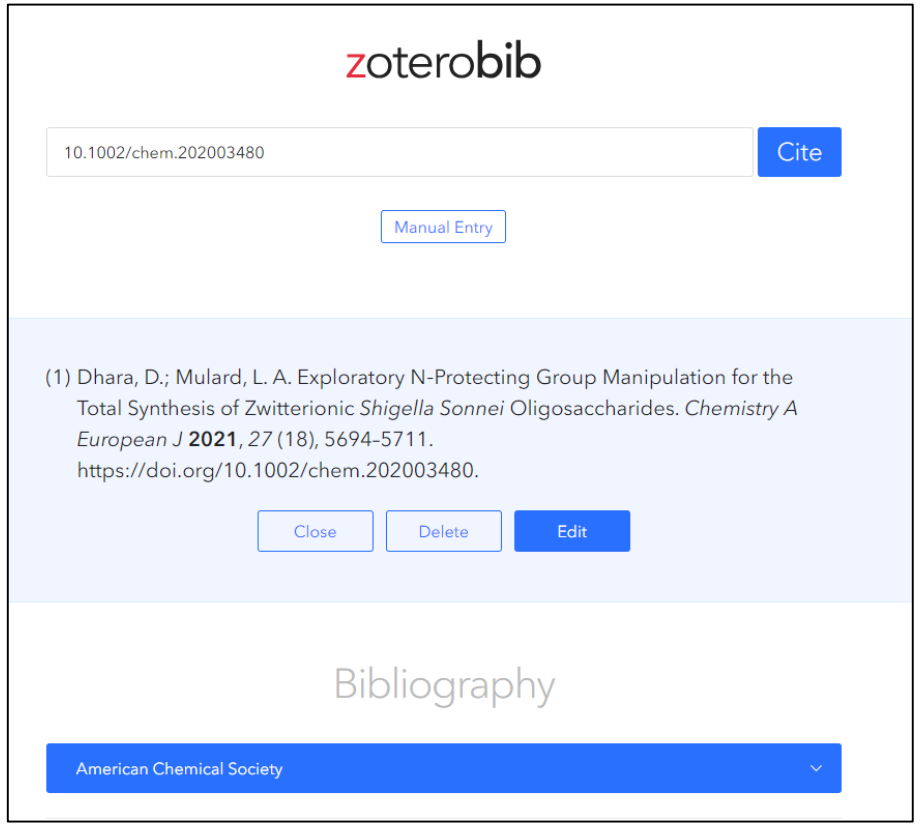
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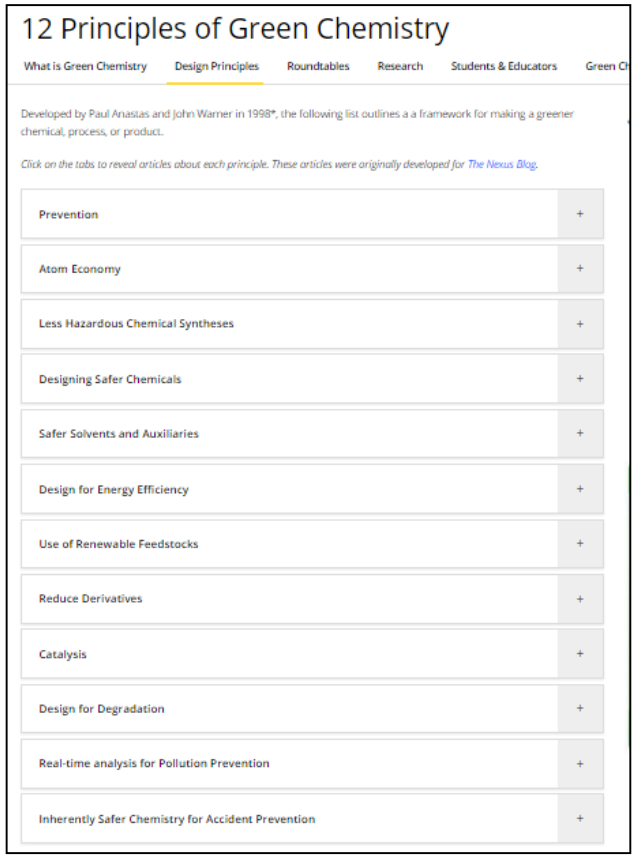
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Safer Solvents and Auxiliaries
Design for Energy Efficiency
Use of Renewable Feedstocks
Reduce Derivatives
Catalysis
Design for Degradation
Real-time analysis for Pollution Prevention
Inherently Safer Chemistry for Accident Prevention

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The 12 Principles of Green Chemistry
Provides a framework for learning about green chemistry and designing or improving materials, products, processes and systems.
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2. Atom Economy
3. Less Hazardous Synthesis
4. Design Benign Chemicals
5. Benign Solvents & Auxiliaries
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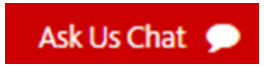

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